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KOCH'S REMEDY
IN RELATION SPECIALLY TO
THROAT CONSUMPTION

LENNOX BROWNE

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KOCH'S REMEDY

IN RELATION SPECIALLY TO

THROAT CONSUMPTION.

BY

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AUTHOR OF 'THE THROAT AND NOSE, AND THEIR DISEASES,' ETC.

ILLUSTRATED BY THIRTY-ONE CASES

AND BY

FIFTY ORIGINAL ENGRAVINGS AND DIAGRAMS.

'So long as the only point of importance was to judge of the correctness of my statements it was not essential to know what the remedy contains and what its origin is. On the contrary, it was clear that subsequent experiments would be all the more unprejudiced the less was known of the remedy itself.'—PROF. ROBERT KOCH,
January 15, 1891.

L O N D O N :

B A I L L I È R E , T I N D A L L , A N D C O X .

P A R I S : B A I L L I È R E . M A D R I D : B A I L L Y - B A I L L I È R E .

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P R E F A C E.

THE unprecedented interest that has been awakened in the world at large by Professor Koch's announcement that he had discovered a remedy for tuberculosis is easy to understand, but the fact that, although its nature is still a secret, his lymph has been accepted as worthy of experiment by members of the medical profession all over the globe, is due solely to his established reputation as the esteemed possessor of every high quality which is held to characterize the true scientist.

For reasons which appear in the early pages of this essay, it is believed that the local effects on reaction of the remedy, can be more advantageously observed in the throat and larynx than on the skin or skeletal joints. To impress this point is my *first* aim.

Secondly, but of not less importance, is the circumstance that from the therapeutic, as well as from the diagnostic point of view, the value of the remedy has been stated by many competent observers to be more satisfactorily gauged in the larynx than in any other internal organ. The reports of the cases which I have witnessed, and of those I have treated, may assist others to form their conclusions on this postulate.

Thirdly, I have endeavoured to explain the general phenomena of the remedy, and the details of its administration, with such fulness as to make the book serviceable to all who desire to adopt the treatment, irrespective of the special organ or structure that may be attacked.

I am fully aware that the ultimate position which Dr. Koch's discovery must hold in the estimation of the medical world cannot be determined for many months, it may be years, to come; and whilst claiming to speak with some authority as to the action of the remedy on the upper respiratory passages, I do not for a moment presume to adjudicate on the final question of its immediate or remote effectiveness on tuberculosis either there or in other situations.

At the present date the discovery is emerging from the stage of unreasonable incredulity and antagonism which was the inevitable rebound of its somewhat premature and restricted announcement, as well as of the hysterical enthusiasm with which it was first received. We are now approaching the calmer sphere of scientific controversy, and it is in this spirit that I venture to offer the first fruits of my observation and experience.

With this purpose in view I have been careful to confine both the indications for, and the expectations of the treatment, within the well-defined limits of Professor Koch's own published communications, and I have, wherever possible, quoted his very words as the text of my opinions, believing that it is only by a rigorous obedience to his precepts that the remedy can be assured a fair trial, and the anticipations of our patients be founded on a reasonably hopeful basis.

The literature of the subject is already so abundantly

prolific and so widely scattered that to enumerate all the authorities in support of many of the statements herein contained, would be to give a list of nearly every medical journal in Europe.

I must, however, make a special exception, by recording my indebtedness to the valuable 'Epitome of Current Literature,' which is issued as a weekly supplement to the *British Medical Journal*.

My thanks are due to the many Berlin physicians who afforded me facilities for seeing their cases during my stay in that city, of whom I would particularly mention Professor Gerhardt, Professor H. Krause, and their respective assistants.

It is also a pleasurable duty to acknowledge the aid afforded me in the histological portion of the book by Mr. Wyatt Wingrave, and likewise the accuracy with which he has recorded the clinical facts of my own cases in his joint capacity of Pathologist and Registrar of the hospital in which they have been treated.

36, WEYMOUTH STREET, W.,
January, 1891.

POSTSCRIPT.

SUBSEQUENT to the final revision of these pages, a detailed account of the nature of Professor Koch's fluid has been given to the world. Of this account it is sufficient to say that the interest of its subject-matter is only equalled by the completeness of the justification for the delay in its publication.

So far, however, from this communication necessitating any alteration in the position I have taken with regard to the remedy, I feel, on the contrary, all the less hesitation in thus early presenting my own views, inasmuch as they are 'unprejudiced' by any foreknowledge of the sealed orders under which we have been sailing.

I am fortunate in being able to print Professor Koch's latest article as an Appendix. Its inherent value is a sufficient plea for its insertion.

L. B.

January 16, 1891.

KOCH'S REMEDY
IN RELATION TO
THROAT CONSUMPTION.

CHAPTER I.

THE CLINICAL HISTORY OF LARYNGEAL TUBERCULOSIS.—
NATURAL, MODIFIED, AND INDUCED.

IN the first edition of 'The Throat and its Diseases,' published in May, 1878, four years before the ever-memorable discovery by Koch of the *tubercle bacillus*, I ventured to insist on the eminently characteristic distinctions of the laryngeal inflammations which occur from time to time in the tuberculous subject; and although there was at that date no absolute evidence of such a condition as a **primary laryngeal tuberculosis**—that is to say, a **throat consumption** which had preceded a similar process in the lungs—I contended that it was 'at least fair to infer that in those cases in which the eye reveals what has come to be recognised as tuberculous laryngitis before the ear detects the presence of tubercle in the lungs, the disease has primarily attacked the former organ. . . .'

'It is quite certain that the pale, opaque tumefactions of the arytenoid cartilages and of the epiglottis in laryngeal

phthisis has not the clear transparency of serous œdema, the active glandular inflammation of simple laryngitis, the hyperplastic infiltration of syphilis, or the angry inflammatory irritation of carcinomia.

'Nor is the consequent ulcerative process less distinctive; there is no erosion, nor deeply excavated circumscribed ulcers, followed by narrowing cicatrices, nor new formations taking on an ulcerative process, but a true carious degeneration, causing loss of tissue, which, commencing superficially at some points, leads to universal destruction of the deeper parts, without extension to the neighbouring glands, and with but feeble, if any, attempt, under treatment, at reparation.'

On these grounds I dared to express surprise 'that we should be told, with reference to laryngeal phthisis, on the one hand, that "tubercl^e appears to play a very secondary part, if any at all," in its production' (Morell Mackenzie); and, on the other, 'that neither the catarrh nor the ulceration of phthisical subjects presents any characteristic signs by which it could be recognised as such, and that attempts made to establish pathognomonic peculiarities cannot be said to have succeeded' (Von Ziemssen).

Finally, I expressed preference for adopting 'the view of Virchow, who just exactly recommends the larynx as the most appropriate place for the study of true tubercle' (*Op. cit.*, p. 222, and third edition, pp. 397, 398).

Since that time the accumulation of evidence has tended to prove almost beyond dispute—

1. That a bacillus characteristic of tubercle is always present wherever the laryngeal appearances are of the nature briefly summarized above.
2. That not only does tubercle play a primary part in

the production of laryngeal phthisis, but that certain peculiarities which are positively pathognomonic almost invariably exist in each case.

3. That although comparatively very rare, there *is* such a condition as a *primary* laryngeal tuberculosis, and that for all purposes of study it may be so considered.

I now desire to advance a corollary to the proposition of Virchow, and to urge that not only is the larynx the most appropriate place for the study of true tubercle, but that it is also the most appropriate and convenient site for accurate observation of the various stages of its development towards reparation which takes place under Koch's treatment.

I shall require to speak frequently of the likenesses and differences of tuberculous laryngitis as it arises in the natural course of disease; in relation to its modification by Koch's remedy; and to its fresh development, or at least the arousing of a dormant tubercular deposit into activity, under this same process, in a larynx previously believed to be sound. I shall, for the sake of convenience, employ the terms *natural*, *modified*, and *induced* to the tuberculosis relating respectively to these three varied states.

In the second edition of my book, published in May, 1887, the relation of *lupus* in the throat and larynx to tubercle received the prominent attention which the increased notice it had attracted in the intervening years demanded. It was shown that lupus in the upper air-passages is much more frequent than has been generally supposed, and that its non-recognition by dermatologists is in a measure justified by the fact that in lupus there is almost uniformly a conspicuous absence of that pain and

local disturbance which is so eminently characteristic of every attempt at a functional act in the case of laryngeal phthisis.

The following paragraph represents the general position still taken on this point by skin-specialists :

Speaking of the desirability of giving a very small dose as a commencement of Koch's treatment in cases in which 'the tuberculosis is of great extent,' a dermatologist of note, writing of a visit to Berlin in the *Lancet* of November 22, 1890, advises the same as 'probably' applicable also to 'lupus in the larynx, where much swelling would be dangerous. He says probably, because as far as he could hear, while laryngeal phthisis had been treated by Koch's method, no case of lupus of the larynx had come under observation; but Koch himself told him that he did not think there would be the same proportion of swelling in the throat as there is in the skin;'

the last being a statement, like all of Koch's, which is verified by experience. But as to those that precede it, I may say that of only three cases of lupus which I saw in Berlin I detected lupus in the uvula in one case under treatment by Dr. Cornet for lupus of the nose, which had not previously been observed, and that extension to both larynx and soft palate had been noted in another case under the care of Professor Gerhardt. Out of five cases of lupus of the face which I have at present under treatment by Koch's method, there is evidence of long-standing laryngeal infiltration in three, and fresh development in one.

Chiari and Riehl insisted on this association of lupus of the throat with lupus of the skin in 1880, and I have recorded that in twenty-five cases of lupus taken in order of observation at a Skin Hospital, either faucial or laryngeal changes, or both, existed in five, though in no instance had the patient been made aware of the fact by any local discomfort. It will therefore be necessary in future for the throat and larynx of all lupus cases to be thoroughly examined both before and during the course of treatment with Koch injections, even if, as I would contend, such a procedure be not admitted as an independent necessary step

towards a complete diagnosis, and irrespective of the treatment to be adopted.

In an endeavour to sum up our present knowledge as to the connection between lupus and tubercle, I said that ‘there are an equal number of eminent observers arrayed both for and against the view that the bacilli of the two diseases are identical; and clinical evidence would appear to show that there is a decided similarity between the two affections.

‘Neisser is of opinion that, “qualitatively (probably), the bacilli are the same, only quantitatively there is a difference, which is intensified by the less favourable nutritive conditions of the cooler skin.”

‘But there are many reasons for supposing that the distinction between the two is not one simply of quantity, for lupus is very little, if at all, more rapid in its progress when it attacks the mucous membrane than when it is manifested in the “cooler” skin; and, moreover, from the vital point of view, tuberculosis is much more universally and rapidly fatal to life than lupus.* . . . The course of lupus is always

* One hears it very commonly said that patients with lupus die of phthisis, but experience of those best qualified to judge is, for the most part, opposed to such an assertion. **Mr. Jonathan Hutchinson** says: ‘It is certainly not common for lupus patients to have definite evidences of tuberculosis of the viscera. I have in the course of many years’ experience known two or three who were the subjects of lupus become affected by aggressive phthisis, but they have been very exceptional. . . . In only 9 per cent. was there reason to suspect phthisis in the individual, and in several of these the evidence was but slight.’ ‘Nevertheless, in spite of his own statistics, he cannot avoid the belief that lupus is, in very many instances, a scrofulous (tuberculous) disease.’—*British Medical Journal*, Jan. 7, 1888.

Mr. Malcolm Morris, in a private letter to me (Dec. 18, 1890), says: ‘I have never seen a case of lupus die of phthisis.’

Dr. Charles Campbell, who has given great attention to the subject, has arrived at a similar conclusion, and has especially pointed out the extreme chronicity of lupus as compared with phthisis.

But it is only right to say that **Leloir**, on the other hand (*Annales de Dermatologie et Syphilis*, vol. vii.), states that of 17 hospital cases treated by him in 1885, 10 showed unmistakable signs of lung tuberculosis.

slow, and while it may possibly, in a few cases—not so few, perhaps, as was formerly believed—terminate in general phthisis (? pulmonary luposis), it more often undergoes a spontaneous process of cure by evolution. . . . The probable truth, then, is that, though perhaps not morphologically distinguishable from that of tubercle, the microbe of lupus is the less powerfully infective both locally and constitutionally, or, as Marty tersely has it, lupus is an “attenuated tuberculosis”’ (*Op. cit.*, third edition, pp. 431, 432).

Finally, in my third edition, published in May, 1890, having had in South Africa an opportunity of seeing several cases of leprosy, attention was directed to that disease as affecting the throat, and granting that lupus might be considered as an ‘attenuated tuberculosis,’ it was suggested that leprosy might represent ‘tuberculosis still more attenuated as regards its slowness of progress and duration, but more virulent in its contagiousness and in the extent of its ravages.’

The histological evidence bearing on these views must be reserved for the next chapter, but as far as lupus is concerned, I shall hope to demonstrate that its behaviour under Koch’s treatment entirely supports the position taken up in the passages quoted.

Reverting now to the course of laryngeal tuberculosis under the influence of Koch’s treatment, I shall endeavour to show, step by step, that every stage in the life-history of the disease, which may extend over *many months, or even years*, can be developed, and, under Koch’s treatment, be compressed into a space of a *few days or, at most, of weeks*, and not only so, but that reparation of ulcers and necroses, which hitherto has been so rare as to be considered by many as almost fortuitous, may take place under the influence of

this magical fluid, with a rapidity which is nothing less than amazing, and afford a series of pictures with actually visible and appreciable changes from day to day.

I would especially ask comparison of the drawings of *modified* or *induced* tuberculosis which accompany this essay, all of them taken from life, and at the bedside of the patient, with those of a more elaborate character, which were selected as typical illustrations of the *natural* disease for my larger work. The similarities are in some cases so exact that the pictures might almost represent duplicate portraits of one and the same larynx.

Commencing with the objective evidences usually seen in the laryngeal mirror as characterizing *natural* laryngeal phthisis, and the likenesses and differences in the *induced* or *modified* forms, it will be convenient to take them in the order observed in my book :

I. Colour.—As a rule, the mucous membrane in the *natural* form is much paler, and of a muddy and greyish hue, except in those comparatively rare examples, of what may be called an *acute* tubercular laryngitis, as distinguished from the more ordinary chronic form of the disease. Under the Koch treatment the natural normal colour is, instead of being paled, invariably heightened, sometimes intensely so, and in some cases to a degree that would render diagnosis not a little difficult to one who for^t the first time saw such a patient in the stage of local reaction, but who should be ignorant of what had been done. In almost all the cases related in this essay attention is drawn to this difference in the surface colour between the *natural* and the Koch *induced* or *modified* forms of laryngeal phthisis.

The hyperæmia is equally constant as a result of the treatment when the disease occurs in the pharynx or fauces.

The same phenomenon of pallor is observed in **lupus**, when the condition represents a long-past stage of active disease; but where laryngeal infiltration is still actively progressing, the colour of the mucous membrane is not much different from the normal, and may be even brighter. Under the influence of Koch injections the colour is, however, always intensified in laryngeal lupus, as in true tuberculosis.

II. Form and Texture.—Commonly, the first laryngeal evidence of *natural* tuberculosis in the mirror is that of deposit (Fig. I.) in the part synonymously defined as the **inter-arytenoid space**, posterior laryngeal wall, or posterior

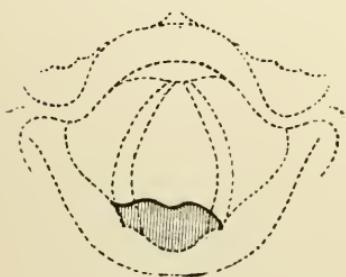


FIG. I.

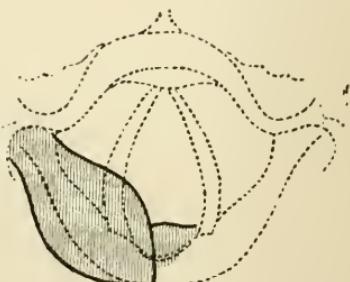


FIG. II.

commissure. (See Figs. XV., XXXIII., XXXIV., and XXXVII.) Following this, 'the well-known and often described swelling of the **arytenoid cartilages** is seen (Fig. II.), giving rise to the appearance of two pear-shaped bodies, the larger ends of which meet in the centre line, and consist of the swollen and no longer distinguishable cartilages of Wrisberg and Santorini, blocking up the hyoid fossa, and tapering off more or less in proportion to the swelling of the aryepiglottic folds until they join the epiglottis.'

See Figs. XXVII., XXXV., and XXXVII., for examples of this condition in *induced* and *modified* tuberculosis.

As a rule, the foregoing described appearance, as well as all other laryngeal evidences of *natural* laryngeal tuberculosis, are bilateral, and more or less symmetrical (Fig. III.), as seen also in the *modified* form in **Case 12** (Fig. XXXI.), but not uniformly so (Fig. III.), as is exceptionally witnessed in both the *natural* and the *modified* examples given in **Cases 15 and 16** (Figs. XXXV. and XXXVI.).

The **epiglottis** takes on a change which renders it quite as unrecognisable to the untrained eye as are the infiltrated arytenoids, etc., just described (Fig. IV.). ‘It becomes so misshapen that no longer is its free edge, superior or inferior

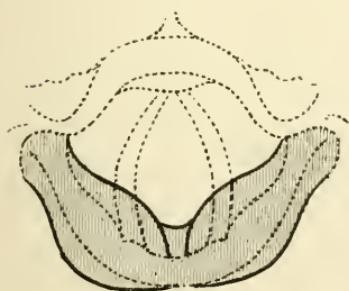


FIG. III.

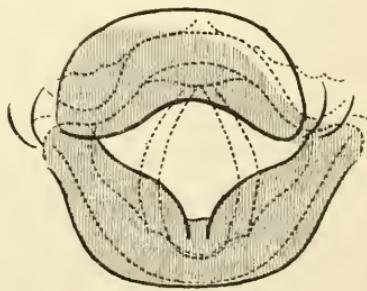


FIG. IV.

surface, or any ligamentous fold, to be distinguished, the whole being swollen into a horseshoe or turban-like shape, which lies nearly horizontally at the base of the tongue, or is so flexed on itself as to resemble a lateral view of the index-finger in a similar position.’ (See Figs. XVI. and XXXI.)

This condition has also been found to take place in the *induced* form (Figs. XXVII. and XXVII*).

In many instances of *induced* or *modified* laryngeal tuberculosis there is not only the infiltration of what may be called the circumferential boundaries of the larynx, but the parts within the vestibule are also infiltrated, and this not

alone in a tumefaction of one or both ventricular bands laterally, in a thickening of the vocal cords, or by sub-glottic œdema leading to a narrowing of the lumen of the glottis (Fig. V.), conditions familiar in the *natural* forms to every expert with the mirror, but there is a levelling, as it were, of the horizontal planes of the larynx, so that the swollen ventricular band is almost on a line with the aryepiglottic fold; the limits of the ventricle itself are obscured, and the loss of definition and contour is such that the relative

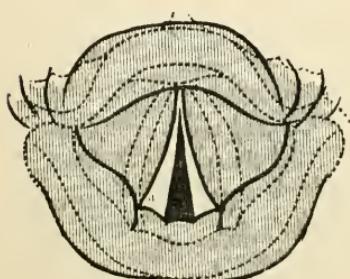


FIG. V.

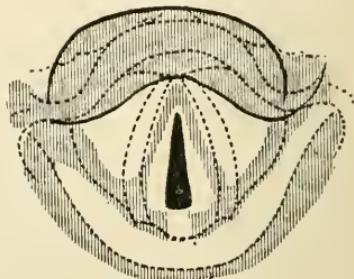


FIG. VI.

distances of parts at various levels are almost obscured (Fig. VI.).

This peculiarity is to be observed in the illustrations, Nos. XXIX. and XLII., and it is to be noted as particularly characteristic of lupus, a unilateral example of which may be seen in Fig. XX., and an excellent one in which there was almost complete supra-glottic stenosis, at page 427, Fig. CXLVII., of my large work.

Not often is this infiltration in the ordinary course of a *natural* tuberculosis of such acuteness as to produce **stenosis**, for before such a complication arises ulceration leading to relief has generally supervened. One such exceptional case (No. 11) I saw under the care of Professor Gerhardt, in which the stenosis occurred two or three days after parturi-

tion in a highly tuberculous patient, and before injections were commenced.

Laryngeal stenosis under the influence of Koch treatment is, however, one of the dangers to be apprehended as an immediate reactionary result of an injection, and is not always to be avoided even by very small, or by only gradual, increase of not too frequently repeated doses. The rationale of such a complication is very simple, and is to be found in the acuteness of the inflammation when *induced* by treatment; but the gravity of the event has been grossly exaggerated, because the most alarming of the reports have emanated from practitioners who, not being specialists, have not been in a position to gauge its degree in the mirror, and to watch its development and subsidence.

And here I would express entire agreement with Professor Krause, whom I heard assert at one of his demonstrations that no one should venture to treat tuberculosis of the throat who is not *au fait* with the laryngoscope. He might have gone further, and claimed that a knowledge of laryngoscopy is indispensable to every disciple of Koch, in view of the possible arousing of a latent tuberculosis of the larynx during the treatment of parts quite remote.

It has been noted that an infiltration of the posterior wall of the larynx—that portion which lies between the two arytenoid cartilages—is at once the earliest and the most usual evidence of laryngeal tuberculosis, and in all probability the cause thereof is that this part is that which is most subject to irritation in functional movements.

[The same fact holds good as explanatory of the partiality of syphilitic deposits for this situation also.]

It is to be further remarked that the cartilaginous portion of the vocal cords, and especially the prominences known as

the vocal processes, are also the portions of these structures that are most constantly the subject of congestion, thickening and ulceration.

This phenomenon is markedly manifested in the Koch *induced* and *modified* inflammations, inasmuch as these are the parts first responding to local reaction. (See Figs. XXXVIII. and XXXIX.)

Ulcerations.—I have been accustomed to describe the ulcers of a *natural* tuberculous laryngitis as peculiarly characteristic in their worm-eaten, carious appearance, which shows that degeneration has not commenced at the surface, but in the deeper lymphoid tissues, which have undergone degeneration, swollen, and given way at the point most favourable for exit of the retained matter, namely, at the surface. These small ulcers then unite by breaking down the intervening tissue, and so form large necrosing areas.

It is but rarely that ulceration of the larynx under the Koch process presents these peculiarities, and I am inclined to think that the cause of the multiple points of exudation characteristic of the ulcers in the *natural* form is due to a difficulty of elimination of necrotic tissue from a deeply situated source, with a consequent death of the surface, first at points of escape and then by a gradual coalescence. On this hypothesis the difference in the elimination of the necrotic material in the *induced* or *modified* form is due to the increased rapidity and intensity, which causes one focus of a general inflammation, rather than the miliary character of the ulceration, indicating the feeble attempts at repair in the *natural* process. It is certainly with comparative rarity that one sees over the swollen epiglottis or arytenoid cartilages in the *induced* form

more than one or at most two points of activity. Several examples of this exception to the *natural* course of ulceration are afforded in my cases.

The colour of these ulcers when Koch *induced* is usually at first white or whitish-grey, with an intensely red areola; and then in a day it is a pale yellow, which might be likened to the deposit of a thin layer of 'laudable' pus, though it is hardly so fluid. This deposit, or, more properly, exudation, represents the elimination of necrotic matter, and to it Professor Gerhardt has applied the term 'Xanthoplasma.'

The appearance is not unlike the *aphthous* ulcer, or, as Virchow has called it, the *lenticular* ulcer, which has been observed not only alongside of tuberculous ulcers, but even alone in phthisical individuals, as well as in the throat affections of the various exanthemata, here again pointing to the probability of their production as the direct result of an active Ptomaine, and accounting for their almost invariable occurrence in connection with Koch *induced* and *modified* tuberculosis of the larynx.

John N. Mackenzie, of Baltimore, U.S.A., in allusion to these so-called *aphthous erosions* of the older writers, thus describes them when present in a case of laryngeal phthisis. 'Their occurrence here is probably explained by the accumulation of irritant sputa,' and he believes that their anatomical appearances, which he describes with his usual care and minuteness, 'leave no room for doubt that these ulcerated areas are the result of a circumscribed superficial diphtheritic inflammation of the mucous membrane; that is to say, an infiltration of its tissues with so rich and rapid cell-proliferation as to eventuate in necrosis and sloughing of the superficial layers.'

I have nothing to add to this description, which so aptly applies to the *induced* ulcers now under consideration, except that the term *necrotic* would be preferable, being less misleading, to the word *diphtheritic*.

When ulcerations of the larynx already exist in a case in which Koch's treatment is pursued, the process appears to have a decided effect on them. At first they are redder, then they are bathed in fluid pus for a day or two, after which they have a cleaner appearance and show a tendency to repair, though completion of the healing is not so rapid as in the case of the *induced* erosions.

In the **pharynx** and **fauces** *induced* tubercular ulcers take on the same multiple characteristics of its *natural* course, explanation of which may be found in anatomical differences of the structures in the two situations. Fig. XVII. illustrates their appearance. As the case progresses they have the same tendency to coalesce that is manifested in the *natural* form (Fig. XXXI.).

Necrosis and Caries are, with the exception of the epiglottis, not often detected during life, although frequently suspected, in *natural* tuberculosis; portions of the thyroid, cricoid, or arytenoid are but rarely extruded, though it is by no means uncommon to find advanced necrotic changes in one or other of these cartilages on autopsy.

In *induced* tuberculosis, the rapidity with which the disease is developed and completed, readily explains the circumstance that death of cartilage has not yet been noted, although extension of perichondinal inflammation may be frequently witnessed. On the other hand, in the curative process, ulceration of the epiglottis has been observed by me to be arrested, and in one recent specimen examined in Berlin was seen to have undergone partial repair. (See Case 17.)

'Sputa.—There has been since the time of Louis considerable speculation and much discussion as to the infective power of the sputa of phthisical patients with cavities in the lungs to produce laryngeal manifestations, and since the discovery of the tubercle bacillus this view has obtained renewed favour. It cannot, however, in our judgment, be maintained, first because our daily clinical experience gives proof that not only tuberculous ulceration, but the tubercle bacilli are to be found in both pharynx and larynx, with almost negative or at least only incipient pulmonary symptoms ; and also because laryngeal evidences are often absent in cases in which there are extensive cavities in the lungs, and this notwithstanding the presence of bacilli in large numbers in both larynx and upper throat. Moreover, tuberculous infiltration, which is one of the earliest and an invariable manifestation of the disease, may proceed to even an extreme stage without there being any breach of surface' (*Op. cit.*, third edition, p. 403).

The correctness of this view is absolutely placed beyond doubt by the rapid appearance of tuberculous infiltration and ulceration in the *apparently normal larynx* and *fauces* of many a patient undergoing Koch injections in the course of what has been believed, at the commencement of treatment, to be a case of uncomplicated pulmonary phthisis or a lupus with absence of throat manifestations. (See Cases 1, 2, 3, and 5.)

This same fact also sets at rest the error which almost all observers have more or less fallen into of regarding **catarrhal** affections of the larynx in tuberculous patients as frequently of a *simple* and *not of specific* character. (See Cases 21 and 22.)

It has to be added that occasionally an area of disease is

aroused not in the larynx but in the **trachea**. Case 15 of subglottic infiltration is one in point, and Case 1 is another; but my friend, Staff-surgeon Dr. Hertel, has recorded several others observed by him in the wards of Professor Gerhardt.

One other point of interest is that of the development of the so-called **new growths** in connection with tuberculous laryngitis. John Mackenzie has expressed the opinion that they may be regarded as representative of a corrective process, and as a natural step towards cicatrization. Holding the same view, I have always deprecated the removal of these little excrescences (for I could not recognise them as true growths), and the manner in which I have seen them become gradually absorbed under the Koch treatment further emphasizes the correctness of John Mackenzie's pathology, and the advisability of a 'masterly inactivity' in regard to them.

In Prof. Von Bergmann's clinic a man with laryngeal tubercle was to be seen ; he had much dyspnea during the reaction, and being seized with a severe fit of coughing, he expectorated a fragment of necrotic tissue, in which giant cells were found on microscopic examination.

So much for a review of the physical signs and objective evidences of the various phenomena to be observed in an ordinary case of laryngeal tuberculosis, and of the facts observed in the Koch treatment. They are of deep interest to all laryngologists if only because they prove all the accepted accounts of the life-history of the disease to have been wonderfully correct. I have also attempted to explain the reasons of certain differences in the character of the phenomena when a tuberculous inflammation is either started or hurried — in other words, in the *induced* or *modified* forms — from what one has seen hitherto in the *natural* course of the malady.

Turning now to the **subjective symptoms**, we shall find

that the parallels of similitude and the points of difference are equally marked and remarkable.

Hoarseness, loss of voice, dysphagia, and suffocating dyspnœa may, under Koch treatment, each and all be induced and subside with a rapidity impressively distinctive from the gradual accession of such symptoms in the ordinary course of the disease, and giving sure anticipation of results which shall present a brilliant contrast to the almost utter hopelessness, or, still worse, the repeated disappointment of hope, which has characterized the use of all our known therapeutic agents and surgical procedures of the immediate past.

One point of considerable interest is the growing **diminution**, under Koch treatment, of that **extreme sensibility** to laryngoscopic examination which is so noticeable in all subjects of laryngeal tuberculosis as to have constituted in my teaching a diagnostic point of some value.

This diminution of sensibility is also displayed in rapid alleviation of the pain attending attempts at swallowing; a striking example of this may be found in the first case of true laryngeal tuberculosis which I have treated by the Koch remedy. (Case 8.)

The patient had suffered from dysphagia of such severe grade that for 17 days he had only taken fluid food, partial anaesthesia being induced by applications of cocaine previous to each attempt at swallowing. The day before the first injection he had even learned the method of swallowing (taught to Wolfenden by one of his patients)—lying on his stomach, and drinking with the head placed at a lower level than the body. On the first day *after* injection (Dec. 15) he asked for and partook of a plate of mutton, and now (Dec. 27) he takes ordinary diet, and has for some days dispensed with the cocaine applications. He even said, with playful boastfulness, that ‘he now prefers crusts.’

Later on there was development of infiltration in other parts of the larynx, and the man again had *difficulty* in swallowing, but he repeatedly said that he never had any recurrence of the *pain*.

Such an almost instantaneous relief, which indeed hardly appears credible, although it is by no means a unique

experience or personal only to myself, cannot thus be early explained by a change in the physical condition, and would seem to imply that some metabolic ptomaine, possessing analgesic properties, has been generated at the seat of the tuberculous inflammation.

CHAPTER II.

HISTOLOGICAL FEATURES OF TUBERCULOSIS AND ITS CONGENERS IN THE THROAT.

HAVING reviewed the general gross indications—physical and subjective—of tuberculous laryngitis, *natural* and *induced*, we will now consider the exact methods, based upon recent scientific experiences, necessary for a further and more complete diagnosis.

Let it first be clearly understood that **tubercle in the larynx** is histologically identical with the same structure wherever else it may occur, and that it consists of a mass of small-cell inflammatory tissue, which is (according to some observers) held together by a filamentous network, and encloses what is known as a giant cell, the whole presenting, more or less, indications of a degenerative process at the centre, whilst it spreads at the periphery, with destruction of the tissue which it invades.

However divided opinions may be respecting the micro-organisms of other specific diseases, there is no longer any doubt whatever of the existence and specific nature of a **bacillus tuberculosis**, the ever - memorable discovery by Koch in 1882 having been since confirmed by all bacteriologists.

Nevertheless, says Koch, ‘ up to the present the evidence of bacilli in the sputum has been considered rather as an

interesting point of secondary importance, which, while it may make diagnosis more certain, is often neglected on the ground that it does not help the patient in any way.' There are even a few physicians who, granting the facts, decline to accept the inevitable deductions therefrom.

Granted, however, that the bacillus is always present in a case of tuberculosis, it does not necessarily follow that it should be found in the sputum in every instance in which the respiratory tract is involved.

But in the minds of many there is still hesitation in accepting the histological identity of lupus and tuberculosis, from a bacteriological point of view; for several careful observers have failed entirely in their efforts to find a specific organism in lupus, and even in those cases in which it has been demonstrated, its specific nature or absolute identity with that of tubercle has been denied.

I have long contended that granting that the bacillus of lupus is morphologically similar to that of tubercle, its behaviour in the living subject proves it to be of far less powerfully infective capability, a view which is supported by the greater benignity of its clinical phenomena, by the difficulty of its cultivation, and by the uncertainty of experimental inoculations. To quote the somewhat quaint expression of a leader-writer in the *Lancet* (December 13, 1890), 'It is very interesting to bear in mind that lupus is, so to say, *the least tubercular* of all these (tuberculous) diseases'; and such is the position taken up by many surgeons, notably by Mr. Jonathan Hutchinson in his Harveian lectures, previously alluded to.

The foregoing remarks apply in a large measure to leprosy, in which disease there is undoubtedly a specific bacillus, grouped in a manner peculiar to the disease,

though individually it bears a strong resemblance to that of tubercle. Attempts at culture of the leprosy bacillus have been even less encouraging than in the case of lupus, since there is no published record of a successful cultivation. Nevertheless, evidence is accumulating in favour of a local reaction in leprosy under Koch's treatment, which is allied to the effect produced by the injections on lupus, and there can be no doubt that the reactionary changes, local and general, which take place under Koch injection, in both lupus and leprosy, have tended greatly to bridge over the difficulties—largely theoretical—in accepting them as congeners of tuberculosis.

One very interesting point must not be overlooked, viz., the great variability in the *number* of bacilli found at different stages and degrees of tuberculous disease, and even at different times of the day. This, however, is doubtless due to the variation in *rapidity* and *extent* of the destructive processes at work; for in cases of so-called chronic or fibroid phthisis lasting many years, bacilli are few and far between, yet, according to most observers, they *are to be found*; whilst in ordinary acute tuberculosis they are ever present in large numbers, but may show daily variations which are extremely marked.

We will now briefly describe the method of demonstrating the bacilli in sputum, the principle of which is the remarkable property of the bacillus of retaining the stain of aniline dyes when subjected to the action of strong mineral acids and alcohol—a property which distinguishes it from all other micro-organisms in either sputum or tissues.

Of the many processes in use, by far the simplest, and the one which gives the most certain and brilliant results, is that known as the Ziehl-Neelsen method.

Having heated to coagulation a thin layer of sputum on a cover-glass, warm a small quantity of the following solution (No. 1), and pour it over the specimen (which is laid in a shallow bath or saucer) :

No. 1.	Fuchsin	1 gramme.
	Carbolic acid	5 c.c.
	Alcohol	10 c.c.
	Distilled water	100 c.c.

Let it remain three to ten minutes, and then wash in a 25 per cent. dilution of sulphuric acid until decolorized. Wash quickly and thoroughly with water so as to remove all acid, transfer to another bath, and pour on the following solution (No. 2) for counterstaining :

No. 2.	Methylene blue	2 grammes.
	Distilled water	100 c.c.

Let it remain one minute, wash in tap-water, dry, and mount in *Zylol-balsam*.

This process has the advantage that it is more permanent than any other, and is equally applicable to tissue specimens ; while the time required is so short that it is in that respect equal to any of the other so-called 'quick' methods.

It, however, oftentimes happens that our search for bacilli in the sputum is unsuccessful when the other evidences are strong. This may be accounted for in some cases by the simple fact that the patient has no expectoration, in others because the disease has no outlet, being, as it were, imprisoned. In the former condition bacilli may occasionally, but not invariably, be demonstrated in the following manner :

Coat a cover-glass or slide with a thin film of hardened gelatine or collodion, place in an oro-nasal respirator over

the patient's mouth for fifteen minutes, remove and stain as above.

Professor Koch's statement that the bacilli 'cannot pass spontaneously into the air from a moist surface' is one that we should greatly hesitate to dispute. Many experiments have been made in this direction, and although the results have proved very variable and questionable, the method of search for bacilli here suggested is one which should always be tried when there is no sputum available for examination; for granting the truth of Koch's assertion, one cannot ignore the fact that they can be occasionally found on the gelatine plates, and whether they are *coughed* up or are simply *exhaled* need not greatly concern us.

A question now naturally presents itself, Have we any histological evidences of quantitative variation in the bacillus in the different conditions of *natural*, *modified*, and *induced* tuberculosis? In the present state of our knowledge I am afraid that we can show nothing of a definite or indisputable nature. If we could, what bearing would this have upon the prognosis?

To this question one may reply that there is no doubt of a diminution of the bacilli in *number* in the sputum under the Koch remedy, but such a circumstance is of itself of doubtful diagnostic or prognostic value, since the same may occur under simple analeptic treatment, or even where no remedial measures whatever are adopted. On the other hand, bacilli may be detected long after the physical and subjective evidences of disease have disappeared; and I may quote the following selected examples from my personal experience, which justify the caution that is necessary in making deductions from such evidence.

The first is that of a man, aged 30, under the care of my colleague, Mr. Jakins, in October, 1890, in whom no bacilli could be found in the sputa, nor even in the

scrapings of an ulceration, diagnosed as tuberculous, which involved the soft palate, fauces, and posterior pharyngeal wall; but on examining a section of the uvula, which was hanging as by a thread, bacilli were found. This patient was also the subject of advanced laryngeal and pulmonary disease, as was demonstrated on autopsy a few weeks later.

A second example I witnessed in Professor Gerhardt's wards at the Charité Hospital at Berlin. The patient, T., æt. 31, was submitted to Koch's treatment on account of suspected tuberculosis, of which a single haemoptysis was the only symptom, there being neither physical sign, cough, sputum, nor bacillus. Commencing with two milligrammes there was no reaction till after the sixth injection, which amounted to two centigrammes. At this date slight dulness with moist râles were detected at the upper part of the right lung, and in the expectoration bacilli were found.

A third case is that of a gentleman, æt. 50, in whom there was very limited disease at the left apex, which had commenced as a sequel to influenza. Of the first specimen of the sputum, which was rather profuse and was slightly discoloured with blood, Mr. Wyatt Wingrave reported the presence of both bacilli and elastic tissue; but three subsequent specimens, examined by this gentleman and also Mr. Walter Fowler, failed to give evidence of either.

Some observations by Koch are of great interest in this connection, since they are about the only reliable information which we possess regarding this variation in the number and distribution of the bacilli in different stages of the disease. He noted that in the early and rapid stage of a tuberculous process, bacilli were present in large numbers, closely packed together, and often *inside* the cells, as in leprosy. But so soon as the highest point of the tubercular process is overstepped, they were *fewer* and *scattered*, many of them being so faintly coloured as to be scarcely visible. These he considers *dead* or *dying* bacilli. When the process comes to a standstill, they finally disappear.

He also remarks that those giant cells which are *free* from bacilli are the *oldest*, whilst those containing *many* are *young ones*.

A further interesting and remarkable statement by the same eminent observer throws considerable light upon some of the other points before alluded to.

‘ It happens that under unfavourable conditions of nutri-

tion, species of bacteria may produce misformed individuals, whilst other qualities, which indeed attract our notice, or interest us from a medical standpoint—e.g., the capacity to grow in the body of a living animal, to evolve certain poisons, etc.—may disappear for a time, or, so far as our experience goes at present, may even become permanently suppressed' (*Bacteriology*, translated by Hime. Baillière, 1890, p. 6).

This harmonizes with the stated variation in appearance of the bacilli in cases of tuberculosis under Koch's treatment; it also explains the occasional absence of clinical phenomena, whilst bacilli are still discharged by the patient.

One highly important influence upon the life-history of the bacillus is alluded to in the same masterly lecture, viz., that of sunlight, direct or diffused, which actually *kills* bacteria. This, however, is a matter for therapeutic consideration, both prophylactic and curative.

According to Gaffsky, bacilli have entirely disappeared from the sputum in a case of well-marked phthisis in four weeks under Koch's treatment. The same has happened to two cases under Guttmann after two months of treatment. Fraentzel has reported a similar result in two cases also after eight weeks' employment of the remedy, but in these there is a record of an occasional reappearance.

If we are to consider that the number of bacilli bears any relation to the intensity of the process, these facts are of the utmost importance; but we must not overlook the circumstance that, so long as bacilli are present, whether perfect or misformed, the patient is still liable to a re-awakening of the tubercular processes.

In addition to the bacillary evidence of tubercle, lupus and leprosy, we must also add that of **giant-cell** formation.

which, as noted in our preliminary definition, is characteristic of a tubercular process, notwithstanding that it may be found in other inflammatory tissues. It is, however, a by no means constant associate of tubercle, and is still less frequently to be found in lupus. It rarely exists apart from the bacilli, which are seen embedded in its substance.

Case 24 may be instanced for what it is worth, as an illustration of the presence of giant-cell tissue, with a presumed absence of bacilli. I had the advantage of examining



FIG. VII.—TUBERCULAR LARYNGITIS.

Vertical section through left vocal cord, showing the tuberculous process in an early stage, consisting of small-cell tissue and giant-cell formation. The epithelium is at present undisturbed ($\frac{1}{2}$ in. objective).

the patient on two or three occasions, and am happy to give in my adhesion to the *clinical* grounds on which Professor Krause's opinion was based.

There are many theories as to the origin of giant cells, the two most worthy of consideration are: 1, that the giant cell is formed by the fusion of numerous phagocytes, invaginating and enclosing a cluster of bacilli; 2, that of Watson Cheyne, who believes that it originates in a bloodvessel

obliterated by endothelial proliferation, and around this focus is arranged small-cell tissue, the whole constituting a tubercle.

In the early period of the life-history of a giant cell, as Koch has demonstrated, bacilli are frequently found in its interior, as shown in Fig. VIII. Later on they are found scattered about amongst the surrounding small-cell tissue.

The **bacillus**, as usually seen in an **active tuberculosis**, presents the following features: It is a rod-like body from



FIG. VIII.—GIANT-CELL GROWTH.

A large-branched homogeneous colloid-looking mass, containing a few bacilli, and surrounded by a zone of large oval-shaped nuclei. Beyond the circumferential clear space small-cell tissue is seen in a more or less cloudy state ($\frac{1}{10}$ in. objective).

$\frac{3}{1000}$ inch to $\frac{1}{12000}$ inch in length, with rounded ends, straight or curved (Fig. IX.).

In sputum it is generally larger than in cultivation. With a high power four to eight spores may be seen in its interior.

Its distribution has been previously referred to.

It greedily retains most aniline stains, and does not react to Weigert's colour test.

In **lupus** giant-cell tissue is also to be seen, but less frequently than in ordinary tuberculosis. Fig. X. shows the process in a typical manner, small-cell tissue is seen to be invading the derma, which appears to 'liquefy' under its influence. At the lower part of field a well-marked giant cell is seen. The epidermis has not been yet attacked. Bacilli are so few and far between in lupus-tissue that many deny their existence, although Koch claims to have

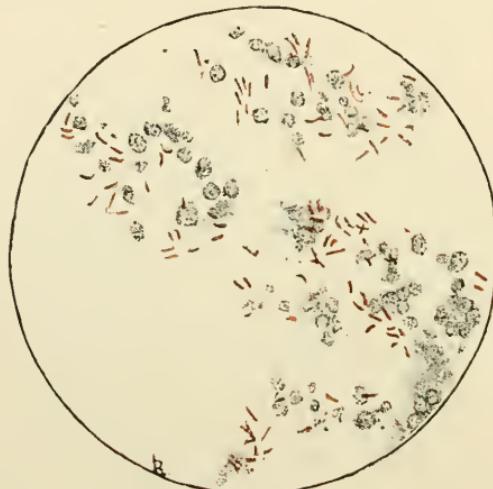


FIG. IX.—BACILLI OF TUBERCLE.

A portion of tuberculous tissue from the ventricular band in case of laryngeal phthisis, stained with fuchsine, counter-stained with methyl blue. The bacilli are seen in large numbers, distributed both in and *amongst* the inflammatory cell tissue, which is in different stages of proliferation and breaking down ($\frac{1}{10}$ in. objective).

found them and made cultivations. They are said to be identical in features with those of tubercle.

The massing of bacilli in **leprosy** is almost a specific feature, and there is no difficulty in recognising the process as it appears in Fig. XI.

Individually the bacilli are very similar to those of tubercle, but are somewhat more slender; their ends are pointed.

In size they are about $\frac{1}{5000}$ inch in length.

They react to Weigert's colour test, and are said to resist



FIG. X.—LUPUS OF SKIN.

An early stage. Epidermis not involved. Small-cell tissue is seen replacing the papillary layer of derma ($\frac{1}{2}$ in. objective).



FIG. XI.—BACILLI OF LEPROSY.

A portion of lepromatous tissue removed from larynx, stained with fuchsine and blue. The bacilli are seen to be clustered in dense masses *inside* and *between* the cells ($\frac{1}{10}$ in. objective).

the influence of Bismark-brown stain; in other respects they are histologically identical with those of tubercle.

Their frequent appearance *inside* the cells, as shown in Fig. XII., is said to be another characteristic and distinguishing feature.

The practical bearing of the histological features of these three diseases is of deep interest. In the early stages of tubercle, the bacilli are intra-cellular, as in leprosy. So long as they remain imprisoned, the progress of the disease is slow; but, whether as a consequence or a cause, its march becomes accelerated so soon as they are released.

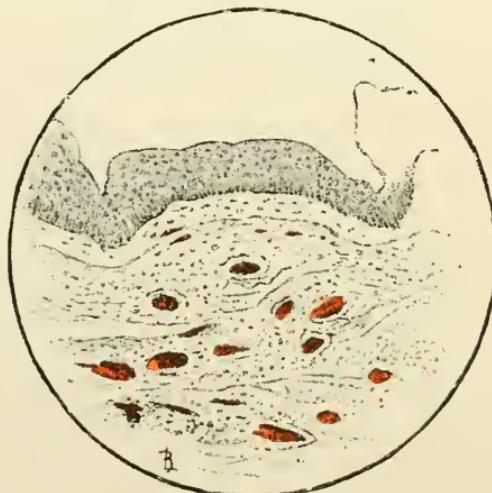


FIG. XII.—LEPROSY OF SKIN.

Shows the ovoid masses or clusters of bacilli, so characteristic of the disease, scattered amongst small round-cell growth. The epidermis not affected ($\frac{1}{2}$ in. objective).

The massing together and closer limitation of the bacilli of a typical leprosy nodule, suggests an interpretation of the slowness of its development, the subsequent devastation of its ravages, and of its contagiousness from open sores. Finally, the sparseness of bacilli in lupus explains the chronic and strictly local character of that form of tubercle.

It is not out of place to add that the differences no less than the similarities in the action of Koch's remedy on these three allied diseases may also be explained on the same basis.

CHAPTER III.

THE RATIONALE OF THE TREATMENT, AS INTERPRETED BY THE CLINICAL PHENOMENA.

THE remedy is a ‘brownish transparent liquid,’ which, although evidently difficult to prepare, ‘does not require special care to prevent decomposition.’ It possesses a glue-like odour, is of somewhat viscid consistency, with a sp. gr. 1150, and is of organic nature. ‘In order to obtain a reliable effect, it must be injected subcutaneously; for use it must be more or less diluted,’ and it is said to be innocuous when taken by the mouth.

The fluid, doubtless, contains a ptomaine, which, possessed of the special property of searching out and precipitating the inflammatory destruction of tuberculous tissue—active or latent—appears to have but little influence on the bacilli themselves. The explanation of this selective action is really simple, for we have a poison sufficiently powerful to influence a *dying tissue*, or at best one of *very slight resistance*, but yet incapable of attacking effectively the original aggressor.

An idea of the extreme potency of the poison may be gained from a statement of Sir Joseph Lister, who was informed by Dr. Koch ‘that the undiluted fluid contains probably only about one-thousandth part of the really active ingredient. If, therefore, one-thousandth of a gramme (which is the ordinary initial dose) is employed, only a millionth of a

gramme of the active substance is used ; yet this almost inconceivably minute quantity, diffused throughout the circulation of the human body, gives rise to effects upon tubercular disease which are . . . *simply astounding*' (*Lancet*, December 13, 1890).

'But,' continues the same authority, 'no such results occur in persons affected with disorders other than tubercular, such as cancer or syphilis. A precisely similar train of febrile symptoms may, indeed, be induced in persons who are not affected with tubercle by using a sufficiently large dose of the fluid ; but for this purpose about a tenth of a gramme is required, or a hundred times the quantity that exists in the first injection in a case of phthisis.' 'But,' to quote the exact words of Dr. Koch, 'the case is very different when the disease is tuberculosis ;' and having described in detail the local and general reactions of the remedy, and its diagnostic value in doubtful cases of tuberculosis, to all of which points I shall return, Koch proceeds to consider, as 'of much greater importance than its diagnostic use, the therapeutic value of the remedy.'

The Rationale of Local Reaction.—The professor considers that 'the local action can be best observed in cases where the tuberculous affection is visible ; for instance, in **lupus** : here changes take place which show the specific anti-tuberculous action of the remedy to a most surprising degree. . . . The observation of a lupus case healed by the remedy is so instructive, and is necessarily so convincing, that those who wish to make a trial of the remedy should, if at all possible, begin with a case of lupus.'

In what way the curative process of the remedy 'occurs cannot as yet be said with certainty, as the necessary histological investigations are not yet complete.' In the descrip-

tion of the changes which a subcutaneous injection of the remedy produces in portions of the skin changed by lupus, Koch mentions 'that after the subsidence of the swelling and decrease of redness, the lupus tissue does not return to its original condition, but that it is destroyed to a greater or less extent, and then disappears. Observation shows that in some parts this result is brought about by the diseased tissue becoming necrotic, even after one sufficient injection, and at a later stage is thrown off as a dead mass. In other parts a disappearance, or, as it were, a melting of the tissues, seems to occur.'

But this is exactly what happens in a tuberculosis of the **larynx**, only in place of the thick external crusts, which in lupus remain for some days before they are thrown off as masks concealing the reparative process underneath, we have the thin 'xantho-plasmic' layer on a laryngeal ulcer, which, quickly disappearing, exposes a surface not subject to changes of the external air, and therefore permitting those accustomed to use the laryngoscope to witness from day to day all the healing stages of a much more active tuberculosis than is lupus, and in a most delicate situation.

In the case of tuberculosis of the **mouth** and **soft palate**, the stages of development and repair may be witnessed with less satisfaction than in the larynx, but devoid of some of the drawbacks pertaining to tuberculous diseases of the skin.

Many of the cases, related in the last chapter, may be taken as examples supporting this thesis.

It is, perhaps, too early to assert definitely regarding the exact nature of the local change brought about by this remedy, beyond the fact that the tuberculous tissue, having been discovered—even in unsuspected situations—is attacked by a powerful poison, which causes its death, and subse-

quently surrounds the bacillary focus by a zone of (inflammatory) protective tissue.

It has been suggested (*Lancet*, December 13, 1890), that the effect of this poison is *not* in direct proportion to the number of bacilli in any given area. This is particularly fortunate, for if otherwise, what a devastating effect it would necessarily have in advanced pulmonary or laryngeal tuberculosis, where it is admitted that the bacilli are vastly more numerous than in lupus of the skin, and where the inflammatory area may be so wide—as in the lungs—or the space for functional duty so reduced—as in the larynx—that the intensity of the process and its attendant phenomena would inevitably prove greater than the resisting power of the patient. But with ordinary care in dosage, it is not probable that either of these dangers would often occur.

It has been stated that the variation of dose required to produce reaction depends on the extent of the disease and on the organ affected. By others this difference has been ascribed to individual susceptibility; but it is much more probable that reactionary effect is due to the proportionate activity of the tuberculous process, and also to the stage of the malady. Thus a far larger dose is required to produce any reaction in the case of a lupus or a leprosy than in a true tuberculosis of the air passages. Similarly the reaction will be more intense when a cavity exists than in the earliest stage of infiltration; while the relation of reaction to any special organ is determined both by anatomical limitations and physiological duties. It is mainly for these reasons that the remedy is so dangerous in the enclosed brain, or in the equally vital kidney.

Coincidently with the occurrence of powerful irritation and its attendant hyperæmia and necrosis, remarkable

analgesic phenomena are manifested in the skin and mucous membrane, to which, in relation to the larynx, I have alluded in the first chapter. Their interpretation is somewhat difficult, and in the present state of our knowledge of the remedy, mainly hypothetical; but we may reasonably infer that this pain-killing property is due to the direct influence of a poison upon the nerve terminals, or—it may be—to the effect of a still further toxic influence developed from the dead or dying tissue, which is the outcome of the remedy.

The fact that this phenomenon does not happen when the disease occurs in joints brings no discredit to the statement, for this apparent contradiction is easily explained. No structures are more painful when inflamed than ligaments, and the increase of pain, which is an almost constant sequel of injection in the case of a tubercular joint, is doubtless solely due to the fact that the invariable hyperæmia and swelling of reaction augments the tension upon a naturally non-elastic, already overstrained, and highly sensitive structure, only partially involved in the tubercular process. Whatever the view taken, all observers are agreed that, rapid as is the occurrence of the inflammation, its duration is proportionally short, and its subsidence almost as sudden as its rise. That the foregoing explanation is correct is strengthened by the facts related in Case 8, in which the rapid relief, after a first injection, of intense distress in swallowing—when there was escape from the already ulcerated surface of a swollen left arytenoid—was followed by a recurrence of difficulty, though *without pain*, when, on a further dose, infiltration occurred on the right side, where the mucous membrane was intact.

It will be quite justifiable and easy, when we have a

little more experience, to remove from the larynx some of the hypertrophic excrescences of which I have spoken under the head of so-called new growths, and recognised by John Mackenzie as tissue of repair; and I doubt not that histological investigation of the phenomena attending the exhibition of Koch's remedy will help to fill up that hiatus in our knowledge of the curative process to which Koch himself has drawn attention.

Koch mentions that 'the remedy does not kill the bacilli, but the tuberculous tissue, and that this gives us clearly and definitely the limits which bound the action of the remedy.'

It appears to me that the fact of the **bacilli** not being destroyed has received somewhat undue importance in the sense that on the disappearance of the bacteria depends the success of the treatment; and this especially in the light of two circumstances: *one*, that no other remedy of an adjuvant character has been employed in the hundreds of cases submitted to experiment in the various hospitals of Berlin; and *two*, that it is quite a common experience to find bacilli present in sputa, which contain no other indication of a destructive process, from patients manifestly recovering, or even recovered, from well-defined disease. Of this circumstance I have seen several examples.

Professor Fräntzel, one of the earliest of Koch's collaborators, has stated that in a considerable number of cases the bacilli disappear altogether, and they always become smaller and thinner, as if they were starved; sometimes they become altered in form, becoming biscuit-like; sometimes they are broken up, or apparently partially disintegrated. This experience, however, has not been yet sufficiently confirmed by other observers to justify a definite statement, and is of the less convincing nature because

such changes in the number and form of the bacilli have been found in even advanced stages of tuberculosis long before the introduction of this new remedy. Altogether the statements as to what become of the bacilli are very conflicting, though there is a general consensus in favour of their decided diminution.

It is fair, therefore, to assume that the diseased tissue, having been all removed, the patient will, under favourable hygienic, climatic and analeptic conditions, be able to resist the influence of such bacilli as remain.

On the other hand, it must be taken as no imputation of failure of the remedy, if the patient, returning to such occupation and surroundings as may have contributed to produce the disease, should have a relapse, which may render the last state as bad, or worse, than the first.

Sir Joseph Lister has already drawn attention to the unlikelihood of **surgical interference** being so frequently necessary for the removal of tissue rendered necrotic by Koch's remedy, as Koch himself has appeared to anticipate; and certainly what may be witnessed in the throat and larynx is most encouraging in this direction. But even were it so, surgical interference in the removal of induced necrotic tissue in the larynx would by no means be so dangerous a proceeding as the ordinary development of a natural tuberculosis, nor of anything like the importance and gravity of the heroic measures which have characterized the recently developed surgery of the lungs.

News already reaches us from Berlin of removal by surgical means of deeply-seated masses of necrotic pulmonary tissue, which have been followed by success markedly greater than that which attended former attempts of a like nature.

From amongst the many valuable observations by

English authorities who have visited Berlin, the interesting impressions of Mr. Frederick Eve on this point are of high value. He says :

‘ Time and further experience have yet to show us how far and in what cases the remedy may be trusted to effect a complete cure, and in what it must be considered only an aid to surgical procedures. These, as Von Bergmann has suggested, will at any rate be of a much simpler and less extensive nature than formerly.’

Mr. Eve concludes by explaining that, while

‘ in superficial tuberculosis, the necrosed fragments are thrown off as a dry scab, in tuberculosis of deep structure the necrotic tissue would probably be absorbed, and shrink in the same manner as tissue affected with coagulative necrosis.’

Unfortunately **immunity against recurrence** has not yet been conferred ; but this probably is only a question of time. The suggestion of Koch, endorsed by Lister, that ‘ when surgical interference is not possible, and when the organism can only help itself by throwing off the tissue slowly, the endangered living tissue must be protected from fresh incursions of the parasites by continuous applications of the remedy,’ is pregnant with hope, and must on no account be forgotten.

Rationale of General Reaction.—In the foregoing remarks I have endeavoured to interpret phenomena within the scope of Koch’s own article as to the local effects of his remedy, particularly in the throat, and this has been comparatively easy, since we are enabled to witness every change in the throat and larynx as it occurs. It becomes, however, far more difficult to attempt an explanation of the general manifestations of reaction, and until our knowledge of the remedy itself is more exact, our interpretations in this direction must be more or less tentative, and the only safe way is to explain them in the light of accepted physiological principles.

Collectively the general phenomena are identical with

those of most other febrile states, due to the direct absorption of a ptomaine; but individually, some of them present features of special interest.

Perhaps, with the exception of the local changes, **the vascular system** is the one which is most profoundly influenced. We have, therefore, first to consider the effects on the heart, the arteries, and the blood itself.

The Heart.—This organ may be influenced in two ways—either through the bulbar centre and its efferent nerves, inhibitory and augmentor, or by direct influence upon the muscular tissue by means of the blood circulating through it. Doubtless both these factors are at work, since not only is the cardio-inhibitory centre disturbed, but also, as one would naturally expect to find, the respiratory, vaso-motor, thermotaxic, and others of less importance. But in the light of recent investigations, explanatory of the influence of certain alkaloids directly upon the muscle substance—*e.g.*, atropin, muscarin, etc.—we can only conclude that the ptomaine of Koch's remedy acts in a similar way, and that it is in fact a muscle poison. We have an analogous condition in the remarkable cardiac effects of the diphtheritic poison to which I believe I was one of the first to draw attention, and of many others, especially the toxic ptomaines of putrescent meat, etc.

The contention that the intrinsic cardiac centres are entirely responsible for the heart-beat has been so conclusively refuted that we may ignore that question entirely.

It may be argued that the cardiac variations are due mainly to increased temperature; possibly that is so, albeit there is often considerable interference, not only with the rhythm, but also with the force and character of the beat, without any marked thermometric change whatever, so that

it is far more difficult to believe in the importance of thermal influence than in that of a direct poison upon the cardiac muscle-fibres such as is witnessed so prominently in diphtheria.

One striking clinical feature, which I have repeatedly verified, is the disproportion in the number of heart-beats and the respiratory movements.

Vaso-motor system.—The remarks on the effects on the heart apply equally to this mechanism. The *bulbar centre* is doubtless greatly influenced, but the change in quality of the blood in circulation, acting directly upon the muscular coat, has a no less important influence on the *arterial tone*.

The correlation of these two factors, combined with a possible alteration in capillary flow (peripheral friction), will necessarily give rise to changes in the blood-pressure. An increase in the force of the heart-beat, with increased peripheral resistance, and contraction of the arterioles, will be marked by a rise in arterial pressure; and this is exactly what we find in the sphygmograms which accompany the cases. This is probably the result when there is moderate reaction, but when it is exceptionally intense, the opposite condition obtains, and we have, as in Case 5, an indication of well-marked low tension and dicrotism, which strikingly contrasts with the healthy tone recorded before an injection was made.

Quality of the Blood.—The changes under this heading are exhibited in various ways, the most important and constant being a diminution of oxy-hæmoglobin, and a slight deficiency in the number of red cells.

The anæmic symptoms appear to vary with the intensity of reaction. In Case 25 there was practically no variation which could be considered due to the injection, but in

Cases 7 and 8, and to a slight extent in Case 6, anæmia was at times well marked, the deficiency of haemoglobin being as much as from 3 to 6 per cent. of the normal, and red cells fell to 4,000,000 per cubic millimetre. Other changes were chiefly the appearance of deformed red cells, increase in white cells, and in platelets.

Similar conditions are found to occur in diphtheria.

It is needless to more than refer to the circumstance that the **Spleen** partakes of, and may be in some measure responsible for, these changes in the blood quality.

Temperature.—Under this heading we shall find much material for reflection.

One very striking result of an injection is the occasional fall of temperature below the normal, and this is to be considered as a sure forerunner of reaction, even in those cases which do not respond to a second or third dose. This fall is, as a rule, at once followed by a well-marked rise, which increases with each successive injection. When response occurs at once, a maximum is generally reached at the third dose.

An inspection of the attached charts will prove interesting and instructive.

The pyrexia of Koch-reaction fever is no less difficult of explanation than is that of other febrile states. Therefore it would be idle to attempt an interpretation in the face of so much contention as to the exact cause of the phenomena of fever generally. At all events, we may be quite certain that it is due to a disturbance of the thermotaxic mechanism; the balance between heat-production and loss being disordered, the vascular and other changes are secondary considerations.

Respiratory System.—Under this heading we have to

notice several phenomena—cough, expectoration, hæmoptysis, and dyspnoea.

Cough is chiefly due to purely local changes in some part of the respiratory tract. In the case of the **larynx** any one of the clinical phenomena noticed in the first chapter would be responsible for irritation, while in the **lungs** we have to expect congestion, more or less localized, and of varying intensity, the re-awakening into activity of a quiescent tuberculosis, or the extension of an existing one.* Lastly, there is the possibility of an arousing of a latent caseous process in the **peri-bronchial glands**, or the establishment therein of an *acute lymphadenitis*. That this condition does arise has been proved by more than one autopsy, and that it is probably more frequent than is generally recognised, is established, not only by physical signs, but by the palpable evidences so often afforded of enlargement of the deep cervical, supra-clavicular, and episternal glands.

Expectoration is always excessive, and is an early evidence of reaction after the first injection, but this is less noted on subsequent occasions. Even in cases in which other indications of beneficial effects are absent, it is rare not to find improvement in the character and in the diminished amount of the sputa, the purulent opacity giving way to a thin, limpid, and frothy mucus. Our experience has so far failed to substantiate the statements of Fraentzel and others as to the constancy of a diminution in number, and an alteration in form of the bacilli.

Hæmoptysis of moderate amount occurred in two of

* Detailed consideration of the pulmonary changes are somewhat beyond the scope of these pages. The reader is referred to a most valuable paper on this subject by Dr. Carl Von Noorden, which appeared in No. 49 of the *Deutsche Medicinische Wochenschrift*, 1890, an abstract translation of which is given in the *Provincial Medical Journal* for February, 1891.

Professor Gerhardt's cases out of a total of forty treated in the Charité, and was in each an early manifestation. It also happened after the fourteenth injection in a gentleman whom I placed under this physician (Case 31). In one other of my patients (Case 9) there was continuance of haemorrhagic streaks in the sputum, which, as in the one last mentioned, had also been a characteristic before the treatment was commenced.

The **dyspnœa** may readily be explained by variations in quantity, quality, and pressure of the blood-supply to the respiratory centre. It might be advanced that further consideration of this interesting phenomenon should be excused on the ground that it refers rather to the effect of the remedy in pulmonary than in laryngeal tuberculosis, always excepting *glottic stenosis* due directly to local infiltration; but in point of fact the anaemia, which is so largely responsible for the dyspnœa, may occur in cases in which the lungs are practically sound.

Kidneys.—Opposed to the experience of many other observers, I have not yet had a case under my own care in which the urine contained either albumen or sugar as a result of the treatment; but the possibility of their presence is by no means difficult to explain, for while increased arterial pressure would account for the albumen, the presence of a poison powerful in its influence upon both renal and hepatic metabolism would equally be responsible for the sugar.

The most characteristic and almost uniform features of the **urine** in my cases have been a deficiency in quantity, in one instance amounting to complete suppression for periods of over twelve hours; and, what has curiously escaped record by others, an abundance of urates, which was followed, as

the reaction passed off, by excess of phosphates. There has further been in every case an excess of urea, indicating tissue-waste, which has persisted through the treatment.

Nervous System.—Amongst the earliest and most constant manifestations of reaction are headache, back-ache, desire to go to bed, and drowsiness without sleep; great prostration on first recovery from reaction, and the feeling of fatigue which may extend into the second or third day. These are by no means, however, to be explained on the hypothesis that they are pure neurosis; but of phenomena that do truly come under this heading, are nausea, vertigo, and occasional vomiting. In one instance this was followed, after a fourth injection of 0·006 grammie and the fifth of 0·008 grammie, by actual delirium, which recurred in a minor degree on successive nights on evening rise of temperature.

Liver.—Slight and transitory icteric evidences have been observed; but whether this is due to hepatic disturbance or to altered quality of the blood, as shown by deficiency of haemoglobin, is not clear.

Cutaneous System.—An early beneficial effect of the treatment is undoubtedly a diminution in the night-sweats, and may be taken as due to central influences. Much has been said concerning the skin-eruptions which vary greatly in character (Cases 6, 7 and 14); and enumerating them in order of severity, they have been described as papular, erythematous, petechial, vesicular, and even pustular. In some instances the rash will only appear after an injection, and then die away; in others there will be a reappearance after successive injections. They do not seem to give rise to any trouble, and are to be noted simply as another evidence of the close similarity of this induced disease with other maladies due to ptomaine poisoning. To the throat specialist these skin-

eruptions are interesting from their similarity to some that I have noted as a sequel to such a simple operation as tonsillotomy, in which the young subject has been operated upon in the out-patient department, and has been afterwards subjected to insanitary home surroundings.

Nutrition.—My experience on this point is in accordance with that of others, namely, that although loss of weight is a necessary result of reaction, a gain is always experienced even between injections with an interval of only a very few days; and the loss is, as a rule, more than compensated for by the increased appetite and general improvement in assimilation.

To sum up, all the foregoing considerations point to the circumstance that the effect of the remedy is strikingly similar to the phenomena attending some of the more severe of the specific fevers; and that, notwithstanding the transitory nature of the reactionary manifestations, the treatment is one which is not to be adopted without the utmost precautions and a just appreciation of the indications afforded by the preceding survey.

CHAPTER IV.

INDICATIONS AND CONTRA-INDICATIONS FOR ADOPTION OF THE TREATMENT.—PROGNOSIS.

SEEING that the opinions of the eminent professors of medicine and surgery who have had comparatively lengthened opportunities of testing Koch's remedy in Berlin, many of them under the immediate guidance of its discoverer, are not yet by any means finite, it cannot be denied that the treatment must for some time longer be considered on its trial, and more especially by those who have recently adopted it in other centres of observation.

From all I saw in Berlin, the limits of selection were varied and elastic, and this, perhaps, to a certain extent was justified ; but it behoves us who live in a country where sentiment so greatly controls scientific research, to say nothing of the ordinary demands of humanity, to do all we can to diminish that distrust which is so apt to surround the introduction of every great scientific discovery, whether that feeling be due to imperfect acquaintance with its principles and technique, or to reasons less honourable.

I therefore propose in this chapter to speak in detail of the guiding principles on which our selection or rejection of a patient should be founded. But the merits of a case must not be considered as dependent solely upon any one of the

following crucial points, which of themselves may vary greatly in importance, but on a broad and comprehensive survey such as any professional man should be equal to.

Age.—Although **lupus** in the face, involving the fauces and upper air passages, may occur at a very early period of life, it does not produce such an amount of constitutional derangement as to preclude us from a recommendation of Koch's treatment, on account of the youth of the patient. In children, however, great care is necessary, for in Professor Langenbuch's *klinik*, a child, $3\frac{1}{2}$ years of age, in whom one-fifth milligram only was given, exhibited a most pronounced reaction, the temperature reaching nearly 105° F.

On the other hand, in no form of tuberculous disease should it be attempted in the old. One of the few fatal cases that has happened in Great Britain was that of a man over 70 years of age, and in chronic ill-health, who succumbed to injections employed on account of lupus in an advanced stage.

The more serious forms of tuberculosis which attack the **throat** and **larynx**—true **throat consumption**—although they occasion very serious disturbance of the vital energies, occur for the most part between early adult and middle life, that is, between 20 and 40 years of age; when the processes of resistance and repair are naturally greatest. I have not yet treated a case of senile laryngeal phthisis by Koch injections, and am even inclined to the opinion that the malady itself is rare, believing that many so-called examples are of the nature of non-tubercular perichondrial changes. But on the whole, I think the rule should obtain with regard to this region that it would be well to observe in all others, viz., not to administer a remedy so potent in its influence upon the higher nerve centres as that of Koch much after middle life.

Habit of Life.—*Alcoholism, plumbism*, and diseases other than tubercular, likely to have been engendered by occupations which have undermined the constitution, must be taken as contra-indications to the adoption of the treatment, or must at least be considered as greatly modifying the hopefulness of our prognosis; for the reason, as in Case 8, and also in Case 3, that the necessary rallying power of the patient may be inadequate. The *syphilitic* dyscrasia, unless constitutional evidences are recent or extreme, is not a contra-indication.

Nutrition.—It being admitted that the evidence gained by alteration in body weight is of great prognostic value in our first examination of any case of throat consumption, it is also to be remembered that gain in that respect is one of our best indications of improvement under analeptic treatment.

Applying these facts to our present subject, we must bear in mind that extreme emaciation is a marked consequence of pain and difficulty in deglutition, and that the beneficial results of Koch treatment are in no instance so impressively manifested as in the relief of deglutitory distress.

Although, therefore, as we have already learned, the immediate effect of this remedy in most cases leads to a further diminution in weight, we must not attach undue contra-indicating importance to the evidence of the scales on the first visit of our patient; for in favourable circumstances we may look for a more than corresponding increase.

Temperature.—The indications afforded by the thermometer are exceedingly valuable, albeit somewhat complex. A moderate elevation of an evening temperature, not exceeding 100° F., need not contra-indicate the adoption of the treatment; but where it exceeds that point, it will be our duty to decide whether the hyperpyrexia depends upon the

acuteness of the process in the larynx (or lungs), or whether it be due to some general disorder amenable to tonic measures. In the first of these conditions injections will be contra-indicated ; in the second they should be delayed.

Night Sweats afford another instance of the beneficial effects of the Koch remedy in their early alleviation under its influence. Nocturnal diaphoresis, therefore, is not of itself to be considered a contra-indication for its adoption, unless it is exciting such a depressing effect on the system as to call for a preliminary course of treatment directed to its diminution ; or unless it indicates, even in the absence of physical signs, the presence of disease, other than in the larynx, of a degree too advanced to offer hopes of success.

Cough and Expectoration.—The remarks in the foregoing paragraph *mutatis mutandis* apply equally to these the earliest and most constant of the symptoms of phthisis.

On the one hand it has to be noted that both cough and expectoration are generally increased a little after the first injection, and then gradually diminishing, in favourable cases, may entirely disappear. But it has also to be remembered that in the character of the cough, and no less in that of the expectoration, are to be found elements of the highest value, from the diagnostic and prognostic point of view.

While the presence of bacilli may, as we have seen, be as profuse, or even more so, in a tubercular pharyngitis or laryngitis, than in the case of a like process in the lungs, the presence or absence of elastic tissue will at once determine whether the disease has extended beyond the sphere of our immediate consideration.

There is a cough accompanying the early forms of laryngeal phthisis which hardly amounts to more than a

desire to clear the throat of an irritation such as would be produced by the relaxation of the uvula, and offers but a very small amount of sputa, which, to the naked eye, is of a quite innocent character, but which on examination may reveal the presence of bacilli.

Such an instance occurred to me recently in the case of a gentleman about thirty-two years of age who had suffered for several months from laryngeal irritation following influenza, and in whom there was no other objective evidence than a very slight infiltration in the posterior wall of the larynx. Sputa were very scanty, and were only to be derived from morning cough on rising from sleep. A specimen submitted to Mr. Wyatt Wingrave afforded undoubted evidence of the presence of bacilli.

Situation of the Local Disease.—With reference to the possibility of easy elimination of tissue when rendered necrotic, this need not influence us much in the case of Consumption of the Throat, for almost all observers have agreed that in that respect the larynx offers special advantages with regard to Koch treatment. Nevertheless, situation seriously modifies our opinion, having regard to the possibility of an **induced stenosis**. It has already been widely taught that previous infiltration in such parts as may diminish the lumen of the glottis is a bar to treatment. But it has to be remembered that not only may such infiltration increase, but that fresh infiltration may supervene on treatment, even when not existing before.

Provided, however, that careful laryngoscopic observation be made before injection, on the alternate days of injection, and especially during the periods of reaction, whenever there be the least increase of dyspnœa, the possibility of this contra-indication is reduced to a minimum, and should be well within the control of any laryngeal surgeon of even moderate attainments in the specialty.

Another point in the situation of the disease to be considered is in relation to the function of swallowing, and we

may here repeat that, although occasionally, by increased œdema of the mucous membrane covering the epiglottis or the arytenoids, deglutition *may* be made more difficult, the contrary effect is the usual rule. In any case, application of cocaine before food-taking, or even artificial feeding, might well be adopted for a day or two, pending the certain reduction of the swelling and the disappearance of the pain which almost invariably follow this treatment.

The extent of local disease may prove a contra-indication, but mainly because it is rare to find tuberculosis of the throat involving mouth, pharynx, and larynx, or at a stage of advanced ulceration in which there are not complications in the lungs or other organs which should make us averse to commencing injections.

The condition of the lungs is the next element of importance, and in giving it consideration I cannot do better than quote the exact words of Professor Koch, since they apply not only to cases in which the lungs alone are attacked, but to those in which the throat is either the primary or the coexistent seat of tubercle :

' Patients with cavities not yet too highly developed improve considerably, and are almost cured ; only in those whose lungs contain many large cavities can no improvement be proved objectively, though even in these cases the expectoration decreases and the subjective conditions improve. These experiences lead me to suppose that phthisis in the beginning can be cured with certainty by this remedy. In part this may be assumed for other cases when not too far advanced ; but patients with large cavities, who almost all suffer from complications caused, for instance, by the incursion of other pus-forming micro-organisms into the cavities, or by incurable pathological changes in other

organs, will probably only obtain lasting benefit from the remedy in exceptional cases. Even such patients, however, were benefited for a time. This seems to prove that in their cases too, the original tuberculous disease is influenced by the remedy in the same manner as in the other cases, but that we are unable to remove the necrotic masses of tissue with the secondary suppuration processes.'

In our present imperfect knowledge of the constitution of the remedy, there are probably few practitioners in England who would be prepared to adopt Koch's treatment in some of the advanced cases of lung disease as here advocated by the professor. Still less should they do so when there is an associated tuberculosis in the throat, for without a doubt, disease in that situation does increase both cough and dyspnœa ; and by causing difficulty of swallowing and of expectoration tends greatly to minimize the chance of success even in the *natural* form and when treated on previously accepted principles.

Rosenbach has said that in considering the treatment of pulmonary phthisis he would, 'as far as possible, select cases with *absolutely unmistakably* physical signs.' So far as the larynx is concerned I would select those in which, the diagnosis being established, disease of the lungs were as *chronic or as limited* as possible. It has also to be remembered that there are, of course, some cases of pulmonary tuberculosis in which the apices being free, the changes are so hidden as to be discovered only with difficulty even by experts, and in such a circumstance an unforeseen pulmonary complication of severe grade may be developed in the course of treatment. The same event may occur by reason of the remedy arousing a latent pulmonary deposit, or the recrudescence of a lesion believed to have been

healed. In cases of laryngeal phthisis with **fibroid changes** in the lungs, my experience would lead me to say that treatment is contra-indicated, or at most should be adopted with very great care.

In one case of which I have knowledge, repeated injections in a patient suffering from old fibroid phthisis *without* laryngeal changes, failed to produce reaction until a centigramme was administered, which produced such alarming results that treatment had to be abruptly terminated.

Pleuritic adhesions, without advanced pulmonary changes, are not necessarily contra-indicative of the treatment, albeit that experience thereof has tended to prove that the majority of cases of pleurisy are tuberculous in their origin.

Enlargement of the bronchial glands should be searched for, and the fact that they may become so actively excited on reaction as to press unduly on the root of the lung must not be overlooked.

Hæmoptysis, if active, is a contra-indication to commencement of treatment, which must be delayed until the hæmorrhage has been subdued; but the circumstance of a slight or remote attack should, *cæteris paribus*, do no more than make us cautious, both with regard to the amount of the initial dose and the interval of the repetition.

Heart.—It has not yet been determined in what forms of cardiac disease injections are safe. In any case this organ should be examined most carefully and assurance made of the non-existence or degree of any organic disease. Functional mischief pointing to serious disorder of the vaso-motor system is to be considered in the light of a contra-indication, or at least as a reason for extreme caution.

Some interesting facts by Hénocque with regard to the diminution in quantity of **oxyhæmoglobin**, as well as our

own experience, as a result of the treatment, would suggest the necessity for examination of the blood before injections were commenced, and if there be marked deficiency of haemoglobin it might be well to give a preliminary course of chalybeates.

The kidneys are reported to have undergone changes during the course of Koch treatment of so grave a nature that examination of the urine both before and during a course of injection must be held as only second in importance to that of the sputum.

The treatment is undoubtedly contra-indicated when the tubercular process has involved the kidneys, and in all cases of well-marked chronic renal disease, especially when attended by dropsy. It need hardly be pointed out with regard to preliminary examination, that albumen may be present without there being of necessity any organic renal mischief.

Internal examination should, as far as possible, be extended to the remaining viscera, it being remembered that jaundice is sometimes a sign of reaction in subjects of all ages, and that diarrhoea, pointing to tuberculosis of the intestines, is often a reactionary result in the case of children. Nor although laryngeal phthisis is so extremely rare in childhood, must the possibility of tubercular disease of the brain or its meninges be overlooked even in a case of lupus. Questions, therefore, as to headache, squinting, vomiting, vertigo, etc., should not be omitted in these instances.

Collective Summary.—However conclusive our opinion as to the suitability of a patient for this treatment may be from an individual experience, or even a series of experiences on one or other form of tuberculosis in the throat, the foregoing considerations plainly demonstrate that

each case must be considered on individual and necessarily variable data; and that only by a collective survey can a just conclusion, favourable or unfavourable, be arrived at. And I must repeat that each day's observation convinces me that until we know something more of the nature, chemical or physiological, of the remedy to be employed, the foundation of our treatment is, with all care in selection, apt to be very insecure.

Let it be granted that the diagnostic and the therapeutic value of the fluid is supreme as applied to lupus of skin or tuberculosis of skeletal joints, and omitting as beyond our scope the possibility of lighting up a latent tuberculosis in the brain or kidney, what are we to say finally with regard to an active tuberculosis of the throat, first in relation to the larynx itself, and secondly, as regards associated pulmonary disease?

i. In the first place, it is to be again noted that a disease which in its natural course is protracted over months or years, and for the most part subacute, is roused into vigorous activity which may compress its duration within a period to be numbered by days.

It is true that in not a few cases, as is to be seen in some of those observed by me in the kliniks of Professors Gerhardt and Krause, and in my own practice, this active course—*e.g.*, in regard to induced formation and repair of ulcers—was most beneficent; but experience has led some to believe that the result is not equally satisfactory where the laryngeal disease has already advanced to the ulcerative stage, in this respect forming a fair comparison with the results of the treatment in the corresponding stages of a pulmonary tuberculosis. On the other hand, Professor B. Fraenkel considers that where ulceration exists there is less danger of stenosis

than in the cases of infiltration alone, as in the former condition there is freer exit for the serous exudation produced in the reaction, and with this opinion I thoroughly concur. This danger of stenosis is increased in cases of infiltration of the structures surrounding the glottis, as, for instance, of the ventricular bands which are situated above, or of the sub-cordal mucous membrane beneath the rima. Again, our cases show that where a sub-mucous infiltration not involving the perichondrium may 'melt away' either with or without ulceration, it is by no means sure that actual perichondrial inflammation will also subside under the influence of the remedy, as it is in the first instance to increase. Moreover, we have seen in one case in our own practice and in one or two in Berlin, that given a perichondrial inflammation of one cartilage, say, of an arytenoid, there is a possibility of setting up a similar condition in the epiglottis which had been previously sound. It is altogether very difficult at present for anyone to make an exact forecast with regard to these possible complications.

But opposed to these sinister suggestions, we have evidence that in some cases there is little or no increase in infiltration though there may be in vascularity, that there is great relief of some of the most distressing symptoms, and that even when a tuberculous process is induced afresh, as it were, in a larynx previously believed to be sound, the same will go on to complete reparation. We are at present equally unable to say in which cases such a favourable course will follow our treatment.

2. As to the lungs, we have already quoted Professor Koch's observations on the effects of the remedy in the various degrees of pulmonary tuberculosis; but, as already hinted, the fact that the treatment searches out *every* tuber-

culous spot may exert an influence, other than benign, on the lungs, and this in two different ways :

- (a) That in which an old cavity, believed to be healed, is roused into a spreading activity, a condition analogous to the re-awakening of shrunken tuberculous glands or the lighting up of an old lupus scar.
- (b) Those cases in which there is a deeply situated cavity not in free communication with a bronchus, and of which the physical signs are very equivocal.

I have seen two cases in which the unfavourable effect of an injection for laryngeal disease, in patients with apparently quiescent lung malady, can only be explained upon one or the other of the above hypotheses.

I do not for a moment forget that Professor Koch has advocated the advisability, indeed the simplicity, of the treatment in the beginning of phthisis, and I trust no one will ignore his earnest warning 'against the conventional and indiscriminate application of the remedy in all cases of tuberculosis.'

But the complications I have suggested, indicate that it is not alone in cases of *advanced* or *extensive disease* that we may anticipate danger, so that both indications and contra-indications for the treatment must for some time to come be uncertain ; and the lesson to be learned from this chapter is that the practitioner who has conducted his preliminary examination with the most thoroughness, and who afterwards proceeds most slowly, will also progress most safely.

PROGNOSIS.

Much of the foregoing refers to the momentous question of the amount of benefit to be expected as well as to its

permanency, both being points fraught with higher practical importance than any other, always excepting the possibility of increasing the malady, or of directly causing or hastening a fatal issue through the agency of the remedy adopted for tuberculosis of the throat.

So far as we know, there has not been any death directly resulting from the remedy in which treatment has been commenced with the minimum dose,* and the indications for caution in repetition have been duly regarded. In one case only, in which such a charge could be at all justified, the patient was so far advanced in pulmonary disease that death could not have been long delayed. All other fatal cases which have been thoughtlessly attributed to the remedy could be accounted for by some such cause, or by cerebral or renal complications which, as we have seen, should contra-indicate adoption of the remedy at all. In simple justice to the remedy, it behoves us all not to attempt the treatment in unsuitable cases, and to exercise the greatest caution in regard to the amount, not only of the first, but of all subsequent doses.

It would, therefore, be only recording the obsolete warnings of past history to draw attention to the circumstance that the early administration by Professor Koch of doses which are now admitted to be dangerous, even in lupus, which is less responsive to its action than is true tuberculosis, arose from the fact that, 'as regards the effect of the remedy on the human patient, it was clear from the beginning of research that in one very important point'—that of amount of dose — 'the human being reacts very

* A reported foreign case, in which death followed in thirty-six hours on a single injection of two milligrammes, might possibly be considered an exception, though I should deem it a *full* initial dose for a girl aged 17.

differently from the animal generally used in experiments—the guinea-pig—a new proof for the experimenter of the all-important law that experiment on animals is not conclusive for the human being, for the human patient proved extraordinarily more sensitive than the guinea-pig as regards the effects of the remedy; and ‘calculated by body-weight the 1,500th part of the quantity, which has no appreciable effect on the guinea-pig, acts powerfully on the human being.’

Beyond this question of direct fatality of a too large initial dose, or of a too frequent repetition, there are several circumstances which should guide us in our dosage from the prognostic point of view. They are :

1. The locality of the disease.
2. The number of foci of disease.
3. The extent of the disease.
4. The intensity of the disease.
5. The stage of the disease—that is to say, whether it be that of infiltration or ulceration.
6. Individual susceptibility.
7. The possibility of accumulation of the remedy in the system.

All these points except the last have already been more or less elaborated in the previous pages, but the last of them is one worthy of most serious consideration. So much has been written about tolerance of the remedy, that the possibility of its possessing a cumulative force in some individuals has been overlooked; but upon this assumption we can easily explain, not only the delay in response to repeated injections, but also the occasional disproportion of progressive increase of reaction to the augmentation of the dose; or again, the more exceptional circumstance of an

apparently sudden reaction to a dose which only exceeds by one milligramme several previous doses which have given no response whatever. The moral is that the dose in true tuberculosis should not, as a rule, be augmented by more than a milligramme until a centigramme has been reached.

Excessively high reaction should always be guarded against, because of its great katabolic influence, and this again brings to our mind the circumstance that prognosis as to life, and no less to success in cure of the disease, depends largely on the condition of the vital energies of the patient when he first comes under our treatment, and indicates the necessity in some cases for a preliminary building up by suitable food and tonics.

Opposed to these considerations of continued progressive and excessive reactions from the prognostic point of view comes the question, Is cessation of reaction to maximum doses to be taken as infallible evidence of a complete arrest of the tuberculous invasion? The answer is not easy. Doubtless in some cases such a circumstance may give us some hope of a permanent cure, but local relapses of lupus have in more than one instance followed so quickly on continued cessation of reaction that the prognostic value of such an event is of itself of questionable value.

As to the particular organ of which this essay treats, the effect of the remedy is undoubtedly beneficial in tuberculosis of the throat, provided the case is taken in hand sufficiently early, and that the lungs or other organs are not too deeply involved. I have elsewhere stated that I have diagnosed with the mirror tubercular laryngitis two years before there were marked evidences of pulmonary disease as revealed by the stethoscope, and with the further power that we now possess in Koch's fluid to make our diagnosis certain it will

in future be culpable not to endeavour to arrest **throat consumption** at its very earliest stages.

But if we cannot cure tuberculosis in the throat, as, on the authority of Koch, we may reasonably hope to do in its early history, we can, as our cases show, promise relief of some of its most distressing phenomena, pain, cough, expectoration, night sweats, and even disorder of voice having been proved to be amenable to the remedy, as a direct result of diminution of infiltration, the healing of ulcers, and even the arrest of perichondrial changes.

As to the question of *relapse* and *immunity*, nothing can be added to what has already been said in Chapter III. when considering the mode in which the remedy acts.

It is clear that fear of the first will be avoided, and hope of the second attained, in proportion as we insist on adoption of 'the methods already recognised as curative, such as mountain climate, fresh air treatment, special diet, etc.,' believing with Professor Koch 'that these therapeutic methods will also be highly advantageous when combined with the new treatment . . . especially in the convalescent stage.'

CHAPTER V.

GENERAL DIRECTIONS FOR THE TREATMENT.

THE following directions, which indicate the measures adopted at my hospital, are detailed as applicable to all cases submitted to Koch's treatment; it being first premised that no patient should be treated except in a hospital, a private medical home, or in circumstances in which the assistance of a skilled nurse can be commanded; for, as is well said by the able Special Commissioner of the *Lancet* (December 13, 1890), 'Facts show most undoubtedly that the properties of the liquid are such as absolutely to preclude its use as an ordinary therapeutical agent in general practice. . . . Several experienced persons, including Von Ziemssen, than whom there is no greater living authority, have expressed strong opinions in the same sense. . . . Further, the selection of cases fit to be treated can only be made, with any hope of success and of avoiding serious danger, by medical men who have studied the question. There are cases in which it would be little short of criminal to commence treatment with injections of Koch's liquid.' In the same letter this writer particularly points to the case of a laryngeal tuberculosis as one in which the complication may be alarming unless treated within easy access of a practitioner able to cope with it; but without myself going so far as is implied in the words quoted, enough has

been said to show that the qualifications of the operator and the surroundings of the patient form an important element of calculation.

On admission, which should be at least two days before commencement of treatment, a careful record of *weight* is to be made, and the *temperature* is to be taken three times a day. A rise of the thermometer above 100° Fahr. at night is to be considered a contra-indication. Equally all the other indications and contra-indications detailed in the previous chapter are to be rigorously considered.

Expectoration and *urine* are to be retained for examination by the pathologist, and the results noted on the **daily ward papers**, an example of which is appended to this chapter. The registrar is to make notes of all physical signs in the *throat*, *larynx*, *thoracic organs*, and *abdominal viscera*, not omitting to take heed of any *neuroses*. Note is to be taken of any *skin eruption*.

The case containing the apparatus is to include, in addition to the bottles containing the injection fluid, two syringes, two conical minim measures and pipettes graduated in milligrammes, two test tubes, a bottle of absolute alcohol, a bottle of distilled water, a small bottle of concentrated carbolic acid, a spirit lamp, and some absorbent wool.

The injection fluid is to be prepared as follows:

One part of the **original fluid**—to be called No. 1—is to be diluted with nine parts of sterilized distilled water, containing half per cent. of carbolic acid, and labelled No. 2. This may be made in a quantity to last a fortnight.

The fluid for use, to be labelled No. 3, is to be prepared by mixing one part of solution No. 2 with nine parts of sterilized distilled water, and should be prepared in quantities estimated as sufficient for two days—in cold weather

for longer. These two last solutions ought to be kept in bottles with paraffin-protected glass stoppers.

The syringes are to be rendered aseptic by carefully cleansing with absolute alcohol, which should never be used for more than one cleansing; the needles are to be kept pure and pervious by the wires passing through them being dipped also in absolute alcohol. Care must be taken



FIG. XIII.—KOCHE'S BALL SYRINGE.

that all the alcohol used for cleansing is driven out of the syringe by evaporation, otherwise changes in the fluid may be produced. It is therefore better to cleanse them with spirit immediately *after* use, and to only rinse with distilled water, and then dry by application of slight heat to the syringe immediately before the next injection.

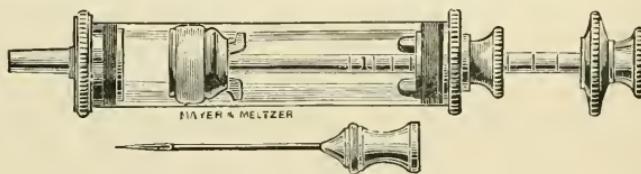


FIG. XIV.—THE OVERLACH SYRINGE.

In the case of *Koch's ball syringe* (Fig. XIII.) the fluid should be poured into the cylinder of the syringe, the end being stopped by the finger, and the ball replaced with the stop-cock turned off. In all cases, one milligramme more than is required should be placed in the syringe, so as to prevent air passing during injection.

If an *Overlach syringe* (Fig. XIV.), in which the piston is made of asbestos, is employed, the fluid should be drawn up

from a measure, into which it has been poured, but not from the bottle. In this case also the amount indrawn should be one milligramme in excess of the requirements.

The best time for administering the injection is in the *early morning*, about an hour after breakfast, as at that time the daily temperature is at its lowest. Opportunity is also thus given to have a good mid-day meal before reaction sets in, the severity of which will in all probability have commenced to subside before the hour for night sleep. In support of this advice I may mention the valuable observation of Rosenbach, of Breslau, that if the injection is made at a time when there is a natural tendency towards decrease of temperature, the fever of reaction does not run so high as when the usual tendency to rise coincides with the effect of the injection.

Preparation of the Patient.—The injection is, preferably, to be made in the skin over the inner and under surface of the shoulder-blade—in the region of the latisimus dorsi—or, in some cases, in the loins, these being the situations of least tactile sensibility, and least likely to be irritated by muscular movements. The sides should be changed from right to left at each injection.

Before injecting, an assistant, whose fingers should have been rinsed in absolute alcohol, is to cleanse the part where the puncture is to be made with alcohol on absorbent cotton-wool, and then again to rub the same surface with a 5 per cent. solution of carbolic acid also on absorbent wool.

The Injection.—Nipping the tissue with thumb and forefinger, the operator is to point his needle downwards and insert it up to the hilt. In the case of the ball syringe, the stopcock should then be turned, and pressure made on the ball. The fluid will pass very slowly, but this is desirable;

therefore, if the piston-syringe is used, gradual pressure, to produce an equally slow exit, is recommended. All the fluid having escaped down to within one drop, the ball-cock should be turned off, the syringe slowly withdrawn, and the injected fluid diffused by a gentle rubbing of the integument.

It is only by such minute precautions in the preparation and injection of the fluid that abscesses, which might prove somewhat serious complications, can be avoided, and the pain, which is almost always felt at the needle wound for the first two or three days, be reduced to a minimum.

Dose.—In no case of **laryngeal disease**, or even of injection for the purpose of diagnosis in a case of suspected laryngeal disease, should more than 1 milligramme (0.001 grm.) be employed for a first injection; that is to say, 1 milligramme of the original fluid (No. 1) as it comes from Koch's laboratory; this amount is represented by a quantity of No. 3 solution sufficient to occupy one of the ten graduations marked on the syringe. The increase of the dose should not be more than 0.001 grm., or another tenth of the syringe for each repetition, until 1 centigramme (0.01 grm. of No. 1) is arrived at, this representing the syringe full of No. 3 to the top of the scale. The amount may be increased from this quantity up to 1 decigramme (0.1 grm.), and this is the dose administered at intervals after a patient is supposed to be cured. When a centigramme, or more, is used, the solution No. 2 may be employed so as not to be obliged to inject so large a bulk. In these circumstances each tenth on the scale of the syringe would represent a centigramme, and ten parts, or the syringe full, a decigramme of No. 1.

In cases of **lupus**, 1 centigramme (0.01 grm.) is permitted by Koch for adults, and half that quantity, or 5 milligrammes

(0·005 grm.) for children under puberty, with further diminution according to age variation. It has to be noted, however, that in many lupus cases there is frequently an unrecognised laryngeal complication, and a disposition to laryngeal infiltration after injection. Laryngoscopic examination should, therefore, be employed in all cases of lupus wherever manifested, and the dose be still further diminished according to any indications thereby afforded of laryngeal involvement.

In leprosy also large doses may be employed to commence with, but as a rule 5 milligrammes (0·005 grm.) would be my maximum dose for a first injection in an adult whatever the malady.

The repetition of a dose must depend on the amount of local and general reaction, of which a fair idea may be gained from inspection of the charts and details of the cases given in the next chapter; but it must be understood that in those cases in which there is a daily pyrexia due to the disease there will only be a fall of temperature after the rise due to the injection equal to that which was observed before the injection was made. This pyrexia of the disease will, however, probably abate concurrently with improvement of other symptoms if the injections take a favourable course. Otherwise this continued hectic must be regarded as a contra-indication for persistence in treatment.

Subsequent Directions.—Unless the patient is really ill, it is not recommended that he go to bed. Indeed, in favourable weather he may go out for an hour or so, provided he is at home within three hours of the injection. The temperature should be taken every four hours, and a note made of every variation, either locally or generally. In view of the rapidity of the changes in the physical con-

ditions of the respiratory passages, it is advisable that daily laryngoscopic examinations should be made, or more frequently as occasion may demand, and the results *graphically* recorded. I would also emphatically endorse Dr. Von Noorden's injunctions as to the importance of a similar daily examination of the chest, marking the area of change and the date on the skin of the patient with indelible pencil.

Referring to the previous chapters for a more detailed account of the effects and possible accidents consequent on an injection, it may be here repeated broadly that the probable indications of reaction will be, *first*, a rise in temperature, which will commence in from five to six hours from the injection; next, a desire to go to bed, which should be at once acted on; and then headache, more or less nausea, possibly slight sickness, pain in the back, a sense of oppression over the chest, and an increase of cough expectoration and local evidences. Accompanying these subjective sensations there will often be observed an excess of urates, and perhaps disorder of the liver. In children diarrhoea may occur, and in two or three days there may appear, quite irrespective of the age of the patient, an eruption on the skin, which may be of various kinds, and have been separately described. Occasioning no discomfort, they require no treatment, and they usually disappear in three or four days.

Of the more important evidences of reaction which call for special watchfulness, are (1) *Cardiac excitement*, indicated by rapid and excessive increase of pulse—though the pulse rise is not regularly proportioned to the increase in temperature—or *cardiac failure*, on cessation of reaction, which may lead to *collapse*. This complication may generally be avoided by commencing with a very small dose at first, and by avoidance of too frequent repetition in those

cases in which the indication is given. (2) *Asthmatic* symptoms, due probably also to cardiac excitement or altered blood quality. (3) *Actual dyspnœa*, due to excess of laryngeal infiltration and consequent stenosis, or to pulmonary causes. These also may generally be avoided by moderation of dose. As a rule, none of the symptoms require more than watching, but there is no objection to the use of restoratives or stimulants, and in the case of a rigor occurring, which is very infrequent, though there is often a sense of chilliness, hot-water bottles, extra blankets, etc., are to be employed.

The urine should be set aside for examination, and also the sputa, which last should be discharged into a glass vessel containing a 5 per cent. solution of carbolic acid. *Expectoration into the handkerchief should be discouraged*, so as to prevent, as far as possible, dissemination of infectious material.

Adjuvant Remedies (Medicinal and Surgical).—In the case of lupus there is no objection to the use of oil, vaseline, or lanoline for the purpose of keeping the incrustations moist. Otherwise it is as well to stop all medicines, such as cough-mixtures containing morphia, or atropine for night-sweats, or any drug which might possibly interfere with the effect of Dr. Koch's remedy. On the other hand, malt extract, cod-liver oil, peptones, etc., which will help to the better assimilation of food and to the making up of loss of tissue, the tendency to which is of course increased by the high temperatures of reaction, are to be encouraged.

In the case of spasmodic dyspnœa, nitrite of amyl might be inhaled, for the purpose of diminishing arterial tension. Cough and pain may be checked by the use of sedative oronasal inhalations.

In laryngeal stenosis the sucking of ice, or the use of a

steam inhalator, with employment of either a hot or cold Leiter coil externally, are indicated. Should instrumental aid be required, I agree with the suggestion of Professor B. Fraenkel that intubation—an operation very easy in the adult—is preferable to the more serious one of tracheotomy.

If there be any increase of local pain in swallowing, topical applications of cocaine, by spray, brush or lozenges, may be permitted; and in case of really extreme odynphagia, nutrient enemata are to be administered, until this symptom is subdued, as it is sure to be in a few days.

It has been asked whether we ought to pursue any other surgical measures in connection with the injections. At present I think not. It is possible that when better acquainted with the remedy, we may scarify or curette infiltrations *induced* or increased on reaction, so as to make a door of escape for necrotic tissue where ulceration has not already provided one. The opinion of Professor Krause, one of the most enthusiastic and successful pioneers in the surgical treatment of laryngeal tuberculosis on this point, is valuable. In my first interview with him, on the occasion of my recent visit to Berlin, I expressed a desire to see some of these cases as well as those under Koch's treatment. His answer was one of regret that that was impossible, for, said he, 'Since this new treatment I no longer use the curette or the lactic acid.' It is not inappropriate to remark that while injections have in one case proved the curative value of Krause's treatment, by the negative results of repeated injections in large doses (Case 29); in another, quoted by Sir Joseph Lister, injections aroused into activity a laryngeal tuberculosis which was believed to have been cured by curetting and lactic acid, the fresh manifestation taking place at the identical spot that had been scraped.

DAILY CLINICAL CHART.

Date..... 189

Name.....

Age.....

Dose.

Diet and Treatment Ordered and Administered.	Time.	Temperature.	Pulse.	Respira- tion.	Sleep. Hours, Min.	Remarks. (Note here details as to Local and General Changes.)	Centigrammes.		Milligrammes.													
							Sputum.	Urine.	10	9	8	7	6	5	4	3	20	19	18	17	16	
9 A.M.																						
10 "																						
11 "																						
12 NOON.																						
1 P.M.																						
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12 MIDNIGHT.																						
1 A.M.																						
2 "																						
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6 "																						
7 "																						
8 "																						

NOTE.—With regard to bacillary evidence, the following abbreviations are used : T.B. $\frac{1}{4}$ represents a large number of Bacilli. T.B. O represents a small number of Bacilli.

T.B. — represents a

CHAPTER VI.

REPORTS AND SUMMARY OF CASES.—CONCLUDING REMARKS.

IN the foregoing chapters reference has frequently been made to the evidence which is to be gained from actual observation of cases of tuberculosis under the influence of Koch's remedy, and with a view of making this testimony easily available to my readers, the cases are arranged under various headings.

1. Those in which tuberculosis was *induced* in situations where it had not been exhibited previously to commencement of the treatment.
2. Those in which existing tuberculosis was *modified* by the treatment.
3. Those in which the treatment was employed mainly for diagnostic purposes.

The Reports include 14 patients I was privileged to observe while in Berlin under **Professor Gerhardt**; 8 under **Professor Krause**; and 9 under present treatment by myself.

CLASS I.

CASE I.—*Lupus of the nose. Induced disease in both larynx and uvula, with healing under treatment* (under Professor Gerhardt).

K., female, single, aged 19, was admitted into the Charité Hospital on account of lupus of the nose, which at the time that I saw her, December 4, was almost well, the skin being of nearly normal colour, free from nodules and ulcerations, and covered by a light layer of desquamating scales. The great interest in this case was that prior to injection the lungs were thought to be quite sound, but

afterwards a well-defined area of dulness was detected in the right lung. In the pharynx also, apparently normal before treatment, there developed in the uvula a nodular growth, about the size of a split pea, which became ulcerated and sloughed off, leaving a hole; this had filled up, and on my visit, beyond very great redness of the uvula and its immediate vicinity, not extending to the pillars of the fauces, there was no morbid evidence whatever. On a second visit the next day the soft palate was of almost natural appearance. The larynx was also believed to be normal, prior to treatment, but after injection there developed an ulcer of the first ring of the trachea just below the anterior commissure, and also a swelling with erosion of a pale yellowish colour at the posterior commissure. The former had healed at my visit, but evidence of the latter lesion remained. There was no longer any purulent coating, but there was distinct roughness, and on phonation the thickening formed a fringe-like obstruction to complete approximation of the cords. There had also been other slight evidences in the vocal cords, which were not noticeable before injections were begun.

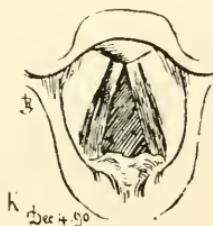


FIG. XV.

CASE 2.—*Lupus of nose, with development of hyperæmia of larynx and ulceration of uvula under treatment (under Dr. Cornet).*

This patient was seen by me casually when going through Professor Krause's wards. The patient, a female, was suffering from lupus of the nose, and was progressing in the course now generally recognised as typical. Dr. Krause had not examined the throat as she was not his patient, but at my request did so; and though there was nothing in the larynx beyond increased hyperæmia, there were to be seen on the uvula, which was highly inflamed, two small ulcerated nodules of a yellow colour.

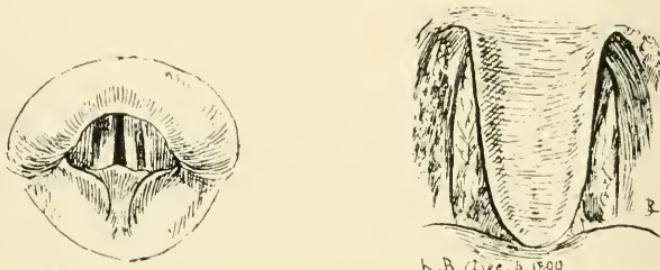
CASE 3.—*Disease of right lung. Subsequent induced disease in larynx after one injection (under Professor Gerhardt).*

F., female, aged 37, married, suffering from pernicious anaemia, with tuberculous infiltration of right lung. Prior to injection nothing abnormal was to be observed in the larynx. After injection on November 28 of 0.001 grammie there was observed a perceptible swelling, almost amounting to a tumour, over the right vocal process. This was now, December 4, decidedly smaller. On account of the very enfeebled state of the patient, no further injections were contemplated, and she died while I was in Berlin. The autopsy threw no special light on the part played by the remedy.

CASE 4.—*Tuberculosis of larynx. Subsequent involvement of pharynx and fauces after sixth injection (under Professor Gerhardt).*

K. B., aged 29, tailor, was admitted into the Charité on November 15, with infiltration of both apices, and had been submitted to seven injections between

November 18 and December 4. In the larynx was typical infiltration of epiglottis, aryepiglottic folds, cartilages, and posterior commissure. Up till the evening of December 5 the pharynx was believed to be healthy, but at that date, some thirty hours after the last injection, there appeared intense œdema of the uvula, and



FIGS. XVI. AND XVII.

great ulceration of a greyish, sloughing character on the posterior aspect of the pharynx, which was at first believed to be diphtheritic, but on the pillars of the fauces, especially the right, numerous spots of lighter and less tenacious ulceration of truly tuberculous character were observed.

CLASS II.

CASE 5.—*Lupus inside right nostril* (under Mr. Lennox Browne).

A. N., aged 30, admitted into the Central London Throat and Ear Hospital January 3, 1891, and transferred to my care by the courtesy of Mr. Jakins.

Family History.—Family gouty. Father has paralysis; no skin disease.

Mother died of typhoid fever. One brother died of Bright's disease, aged 20. Maternal grandfather died of phthisis. One maternal uncle died of phthisis. Grandmother gouty and eczematous.

Personal History.—Typhoid fever when aged 5, measles at 10, followed by abscess in the foot, which discharged for six months; since then has had several more abscesses in the neck and leg, the last being fourteen months ago, in both these situations. At the age of 15 had an attack of 'erysipelas,' i.e., swelling of face, which lasted a week. Since then she has had recurrences of this nature at intervals of a few months, each one leaving the face more swollen. She traces the lupus from these attacks. Has been treated at a Skin Hospital for six months, with benefit. Health has been fairly good. One month ago had an attack of swelling over eyelids and right ear, which was attended by slight constitutional disturbance.

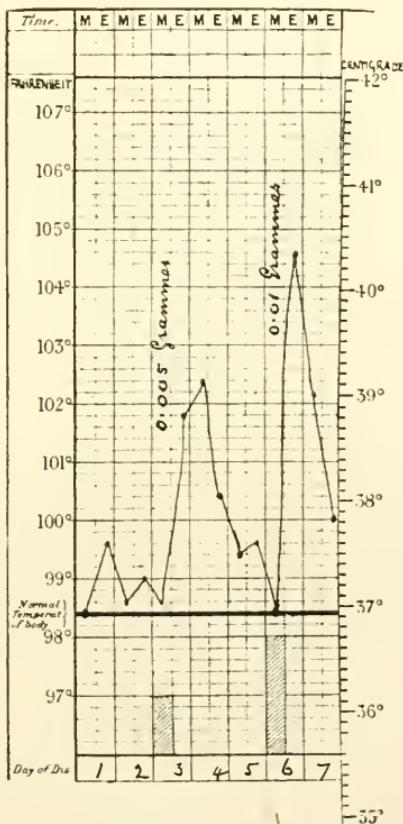
Present Condition.—Complains of a skin disease mainly affecting the nostrils, of fifteen years' standing. There has been no ulceration since twenty-seven years ago, when it was scraped. There is now active ulceration in the right nostril. Elsewhere cicatrization looks firm. Menstrual function irregular and rather excessive. Bowels regular.

Faeces slightly thickened. General congestion of laryngeal mucous membrane, especially over cartilages of Wrisberg. Vocal cords also slightly congested.

Heart and Pulse, normal.

Lung slightly bronchitic.

Temperature.—Morning, normal ; evening, 99.6° F.



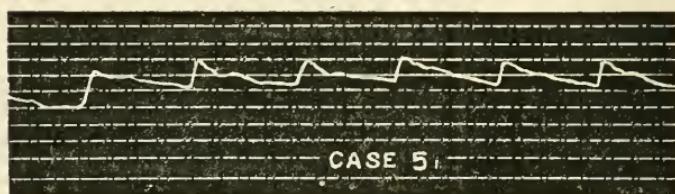
TEMPERATURE CHART OF A. N.—CASE 5.

N.B.—The shaded columns indicate the date and amount of the injection, each square representing one milligramme.

January 6, 10 a.m.—First injection, 0.005 grammie.—9 p.m.: Feels weak and languid ; pain in the back ; no sweating nor sickness ; voice thick and slight cough ; eyelids red and swollen. Lupus scars swollen and red ; nodules very prominent. Highest temperature, fourteen hours after the injection, 102.4° F. Pulse, 108. Respiration, 24. Sphygmographic tracings showed markedly low tension and dicrotism as opposed to the healthy tone before injection.

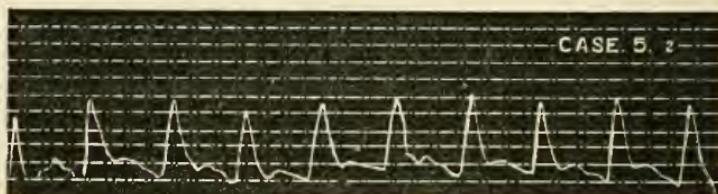
January 7.—The face is very much swollen, and flushed from the limit of the eyebrows to the mouth. There is especially a brawny thickening of the upper lip, on the left side of which, as also on the right cheek, are large and prominently raised nodules over the site of cicatrices. Eyelids very swollen, almost closing the eyes. The face has generally the appearance of an erysipelas.

January 9.—Second injection, 0·01 gramme.—Reaction rapid and intense so far as temperature is concerned, but with comparatively little disturbance otherwise, generally or locally. Highest temperature, 104·6° F.



Pulse-tracing before Injection.

Temp. 99.6° F. ; Pulse 82 ; Resp. 22.



Pulse-tracing during Reaction.

Temp. 102·4° F. ; Pulse 108 ; Resp. 21.

January 10.—Free exudation taking place from inside of right nostril, and on upper lip ; all the rest of the face which had taken the blush on the first injection is desquamating. There are now to be seen on the uvula three distinct nodules, with a zone of hyperæmia and with a point on each of xanthoplasmic deposit.

January 15.—Great improvement in the face. *Third injection, 0·015 gramme.*

CASE 6.—*Lupus of the face, especially the nose and larynx. Re-awakening of dormant areas and great improvement (under Mr. Lennox Browne).*

ALFRED F., aged 18, admitted, December 14, into the Central London Throat and Ear Hospital by the kindness of Dr. C. M. Campbell.

Family History.—Father and mother living, and healthy; five brothers and sisters also living, and healthy.

Personal History.—Lupus on cheek since infancy; lupus on nose two years.

Has been treated by Dr. Campbell since 1887, who found bacilli after repeated sections, but failed to get cultivations. Has had no other disease. Has not lost weight, and no symptomatic indication of throat affection.

State on Admission.—**Face:** Lupus-process active only around the alæ of the nose; septum intact; a pale, glazed and quiescent scar about 2 inches square on the upper part of the right cheek. This represented a large lupus patch, which Dr. Campbell had treated with his special punch, afterwards packing with corrosive sublimate in lanoline (1 in 500).

Fauces: Normal. **Larynx:** The epiglottis greatly infiltrated, and generally of rather heightened colour, except on the surface of an old cicatrix, observed at about the centre. The left aryepiglottic fold and ventricular band apparently matted together. Neither vocal cords seen, on account of swelling of ventricular bands. (Fig. XIX.) **Chest:** Normal. A cicatrix on the back of the right hand represents an ulcerated patch, which healed spontaneously some years ago. **Urine:** Normal. Weight, 8 st. 6 lb.

December 14, 1890.—**First injection, 0·003 grammes.**—General reaction slow, there being no rise in temperature till about twenty hours, when thermometer registered 100° F.; but the nose became swollen and red in six hours, and a dry feeling in the throat was experienced in sixteen hours.

December 15.—**Second injection, 0·0045 grammes.**—Highest temperature ten hours after, 101·2° F. Slight headache and malaise. Urine abundantly charged with urates.

December 16.—Anuria for a few hours. Throat rather sore and feels hot. No change in larynx. Slight papular rash over the back. The nose is very red and swollen, and there is considerable exudation from the ulcers. Three red patches have appeared, one at each angle of the jaw, where there were sores two years ago, which had healed spontaneously, and a third under the chin; this patch was the largest, and was much swollen. It represented the site of a gland which had supplicated two years ago, and which had apparently been quite healed. The appearance of the scar formerly treated by Dr. Campbell was interesting, and afforded very satisfactory evidence of the success of his treatment. The colour was much intensified, and less glazed; at the extreme margin of the upper and outer angle, as well as at the lower and inner, there was very slight desquamation, but there was no breaking out whatever of the main surface of the cicatrized area. The eyelids were red and swollen. The scar on the hand is unaffected.

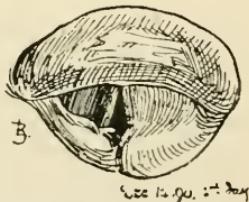


FIG. XVIII.

December 17.—Third injection, 0·006 grammie.—Temperature rose to 100° F. in ten hours. To-day a good view of the larynx was obtained. The right vocal cord was obscured owing to the swelling of the ventricular band and the matting together; the left side of the epiglottis with corresponding aryepiglottic fold, and ventricular band was very plainly to be discerned. (Fig. XIX.) Considerable pain in the throat. Otherwise well.

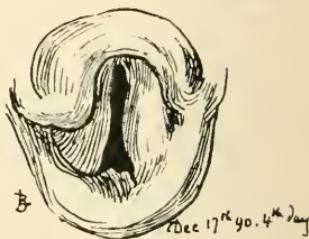
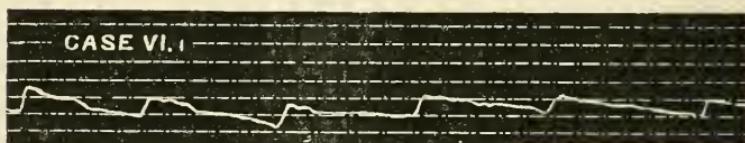


FIG. XIX.

December 19.—Fourth injection, 0·008 grammie. Highest temperature 102·8° F., eleven hours afterwards. Pulse 90. Some pain in the back and head. Urine plentiful with abundance of urates.



Pulse-tracing before Injection.

Temp. 98·6° F.; Pulse 74; Resp. 20.



Pulse-tracing during Reaction.

Temp. 103·0° F.; Pulse 104; Resp. 38.

December 20.—Fresh patches previously noted on face are fading away. Larynx less swollen. On the under surface of the epiglottis, and about the centre a red nodule is seen; the right vocal cord and small portion of the left visible. Both the right cord and the ventricular bands somewhat nodular at the free edges. Anuria for twelve hours. (Fig. XX.)

December 24.—Fifth injection, 0·01 grammie. Slight shivering with headache and sore throat three hours after.

Highest temperature in eleven hours 102° F. Pulse 92. From this time

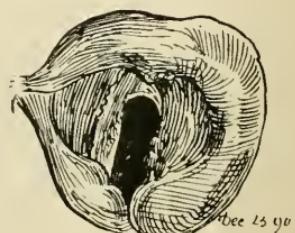
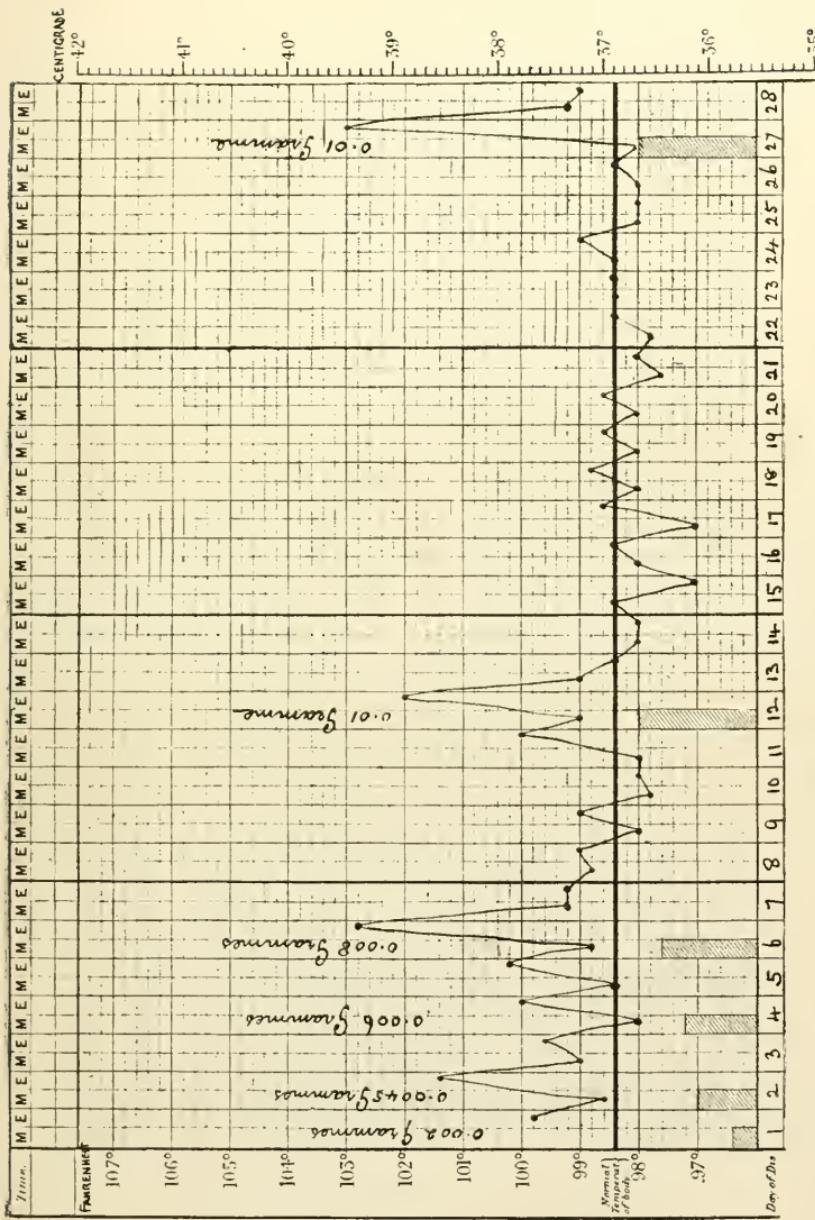


FIG. XX.



TEMPERATURE CHART OF A. F.—CASE 6.

N.B.—The shaded columns indicate the date and amount of the injection, each square representing one milligramme.

no further injection was made till the incrustation over the ulcer on the nose had almost all been shed, which occurred on the 8th day of January. The appearance of the crust on the 21st day is depicted in Fig. XXI. The whole surface was wonderfully better, but there being still one prominent nodule on his left ala, and in view of the state of his larynx on January 9, 1891, a **sixth injection of 0·01 gramme** was made. A pulse-tracing was taken both before injection and eleven hours later at the time of greatest reaction. Highest temperature, 103° F. *Local* reaction much milder. In the meantime he had improved in general health, and whereas he weighed on December 29 8 st. 4 lb., the scales showed on January 5 8 st. 6 lb., which represented a regain of all he had lost.

CASE 7.—*Lupus of the nose, fauces, and larynx. Great improvement (under Mr. Lennox Browne).*

HARRY W., aged 14, admitted December 13 into the Central London Throat and Ear Hospital, and transferred to me by the courtesy of Dr. Orwin.

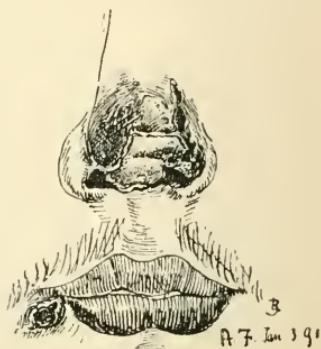


FIG. XXI.
(Half measurements of life.)

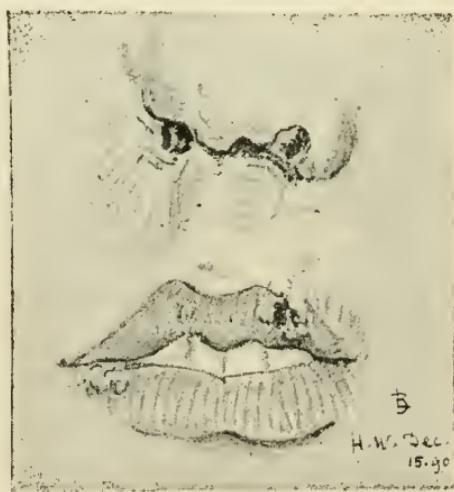
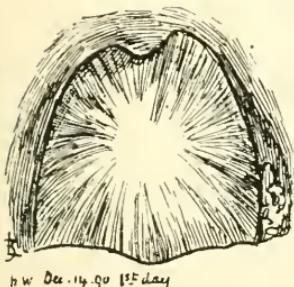


FIG. XXII.

Family History.—Father and mother living, and healthy. Five brothers and sisters also living and in good health.

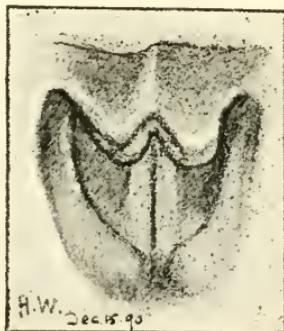
Personal History.—No other disease. Lupus commenced three years ago. Out-patient for one year under Dr. Orwin. Treated with acid nitrate of mercury with great benefit, but with frequent relapses.

State on Admission.—**Face:** Right nostril and ala destroyed by lupus, which is still moderately active here, as well as at left nostril. A few faint nodules on skin at end of nose; several cicatricial scars with thickened tissue at right side. A small lupus ulcer on left side of upper lip, and at angle of lower lip (Fig. XXII.). **Throat:** Uvula and portion of left anterior pillar destroyed by old ulceration. A small flat ulcer of greyish-yellow colour to be seen at site of left tonsil, which is atrophied. A large stellate cicatrix is seen on back wall of pharynx, representing ulceration of old date (Fig. XXIII.). The larynx is red, and the edges of the epiglottis, which is pendulous, are somewhat blunted (Fig. XXIV.).



H.W. Dec. 14. 90 1st day

FIG. XXII.



H.W. Dec. 15. 90

FIG. XXIII.

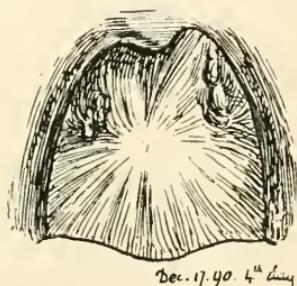
December 14.—First injection, 0·003 grammie.—Highest temperature twelve hours after, 101° F. Head aching and hot; restless; nose red, and somewhat swollen.

December 15.—Second injection, 0·045 grammie.—Highest temperature, 102·6° F., ten hours after. Pain in back and head; soreness and dryness of throat; nose and lips much swollen; urine overcharged with urates and mucus.

December 17.—Third injection, 0·005 grammie.—Slight miliary rash of minute vesicles all over the back; redness of left eyelid. There is also evidence of lupus nodules at the edges of the cicatrix on back of the pharynx (Fig. XXV.). Ulcer at left faucial arch less distinct, being redder. Throat sore and dry. Wakeful and restless, with sweating at night. Highest temperature, ten hours after injection, 103° F.

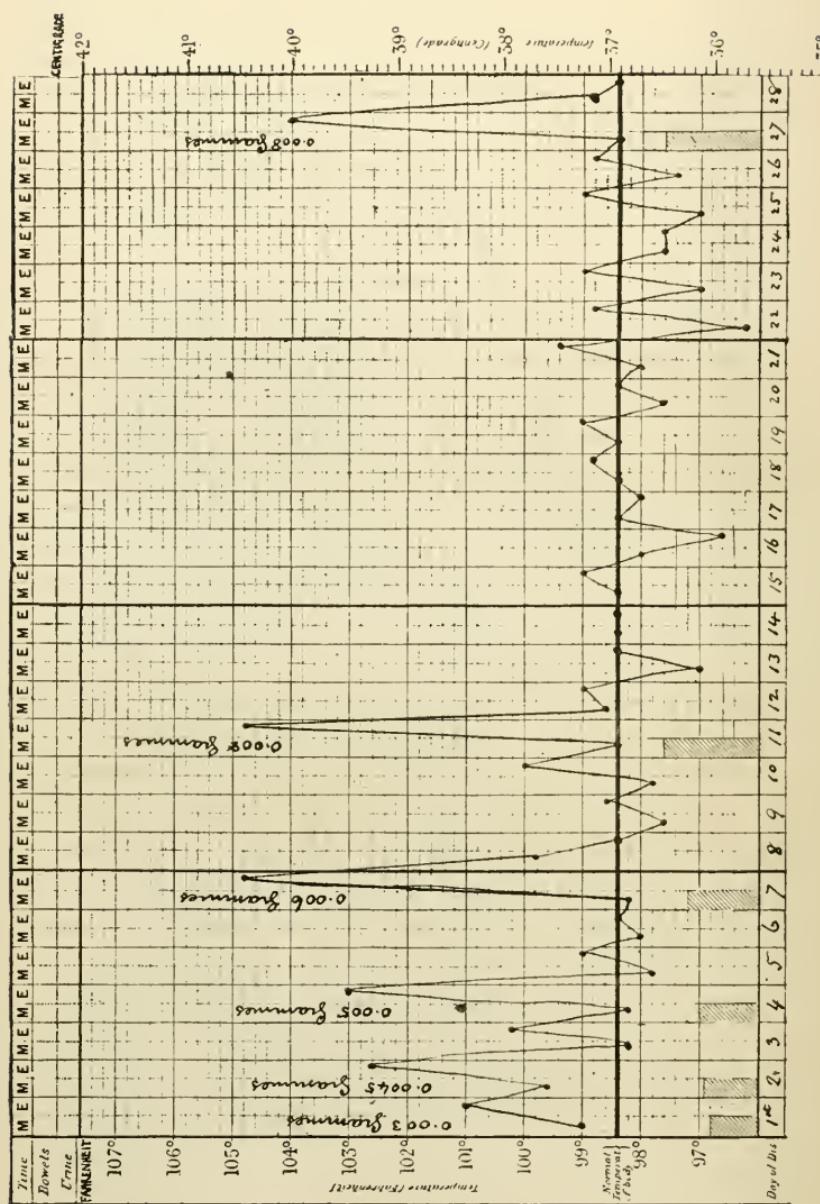
December 18, 8 a.m.—Temperature, 98·4° F.; at noon, subnormal—97·8° F. Inside of upper lip and gums of upper teeth sore. Slight thickening and erosion of inter-arytenoid fold.

December 20.—Fourth injection, 0·006 grammie.—Highest temperature



Dec. 17. 90. 4th day

FIG. XXIV.



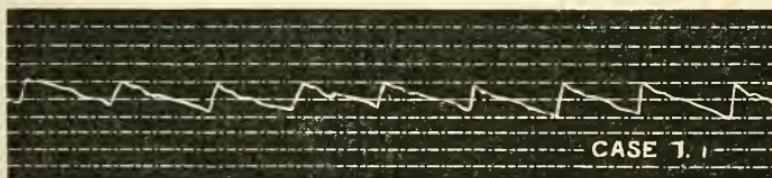
TEMPERATURE CHART OF H. W.—CASE 7.

N.B.—The shaded columns indicate the date and amount of the injection, each square representing one milligramme.

(8 p.m.), ten hours after, 104.8° F.; pulse, 120. During the day great general reaction, with distinct rigor about 4 p.m. Slept well from midnight, but breathing heavily, moaning, and wandering. Skin-rash papular and more marked, being on both chest and back.

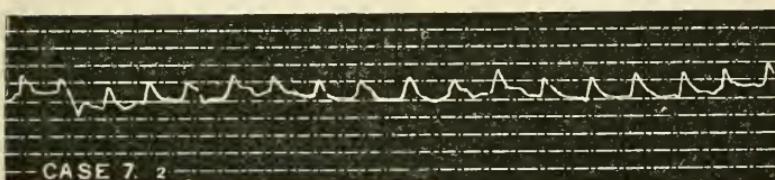
December 21.—Recovering well from reaction. Temperature, 99.8° F. at noon, pulse 104; 97.6° F. at 8 p.m., pulse 82.

December 24.—**Fifth injection, 0.008 grammes.**—Very sick, with headache and shivering at 3 p.m. Highest temperature, ten hours after, being 104.8° F.; pulse, 120; respiration, 52. Restless, heavy breathing, and troublesome cough, without expectoration. Slept all night, but with signs of delirium, as after the last injection.



Pulse-tracing before Injection.

Temp. 99.6° F.; Pulse 80; Resp. 18.



Pulse-tracing during Reaction.

Temp. 104° F.; Pulse 146; Resp. 38.

December 25.—Temperature, 8 a.m., 98.6° F.; pulse, 94. The incrustation being now well formed over both nostrils and lip, no further injections were made till they came away on January 8, 1891, leaving a clean surface, but one by no means free from lupus nodules. Those on the back wall of the pharynx are practically unaffected. In the meantime, he had lost weight up to December 29, when he registered 6 st. $\frac{1}{2}$ lb.; but on January 5, 1891, 6 st. 2 lb.

January 9, 1891.—**Sixth injection, 0.008.**—Reaction more quick, and not quite so intense. Highest temperature, 104° F. Increased redness, but not great swelling nor so much exudation as on previous occasions.

January 10.—Evening temperature normal.

CASE 8.—*Quiescent pulmonary disease. Unilateral tubercular laryngitis; great improvement at first under injections, later extension to the rest of the larynx, and re-awakening of pulmonary disease (under Mr. Lennox Browne).*

HENRY H., aged 32, barman, single, admitted November 26, 1890, into the Central London Throat and Ear Hospital, complaining of sore throat and hoarseness.

Family History.—Parents and grandparents healthy and long-lived; one brother weak in the chest; one maternal uncle died of phthisis.

Personal History.—Healthy till three years ago, when he attended Victoria Park Hospital for chest complaint, which had really troubled him for four years previously. Twelve months ago the throat commenced to be painful, and four months later cough and voice trouble began. Has lost flesh in the last eight months; gradually increasing odynphagia; expectoration very considerable. No haemoptysis. No history of syphilis, but has been decidedly addicted to excess of alcohol.



FIG. XXVI.

State on Admission.—Voice nearly lost; much cough and expectoration.

- Great odynphagia, and no solid food taken for sixteen days previous to admission. Extreme pain even with fluids. Urine normal.

Right Lung.—No marked signs, excepting slight dulness at the apex.

Left Lung.—Some well-marked dulness at the apex; prolonged expiration; no râles; vocal resonance increased.

Expansion deficient on both sides.

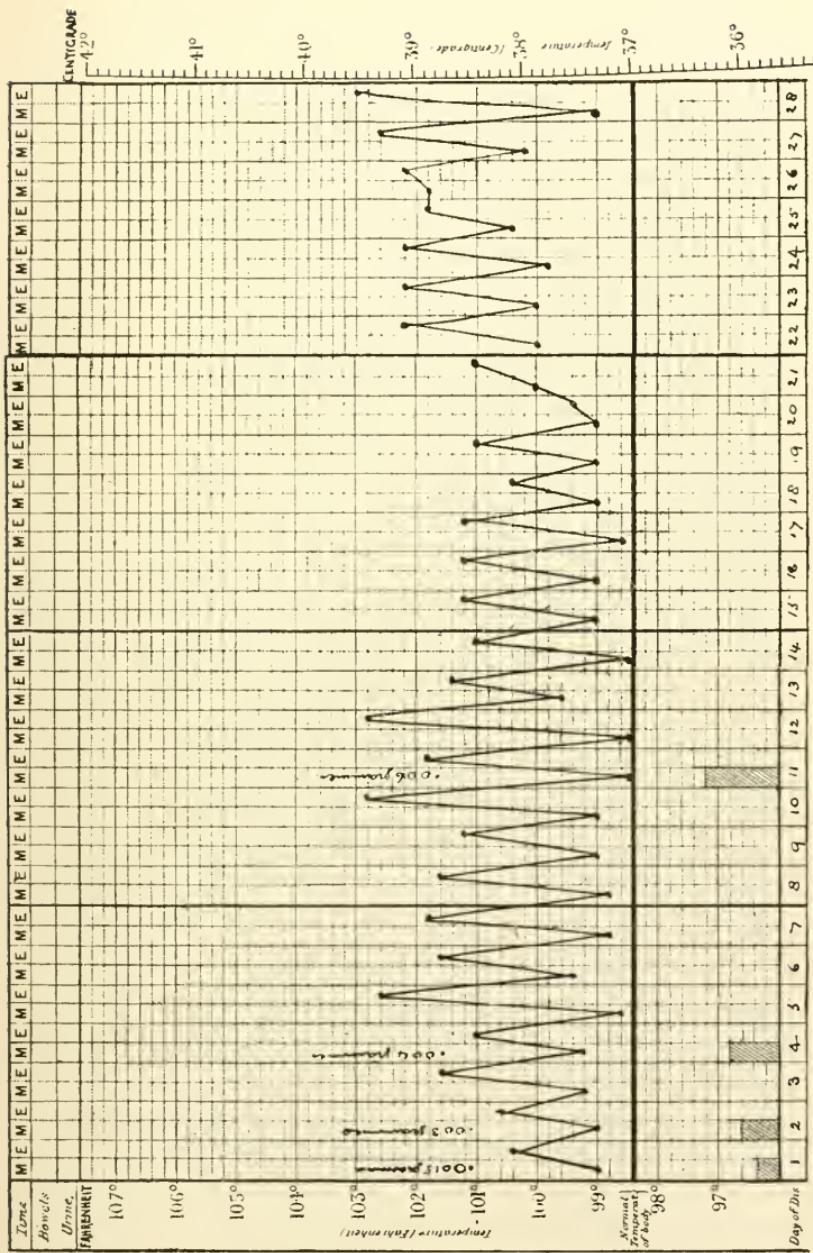
Heart Normal. Temperature, a.m., 99° F.; p.m., 100° F. Weight, 8 st. 8 lb.

Larynx.—Great infiltration of left aryepiglottic folds and of arytenoid cartilage, and of both vocal cords; ulcerations on these structures and on ventricular bands. Epiglottis normal. Sputum profuse; no elastic tissue. **Bacilli** fairly numerous.

December 14.—**First injection, 0·0015 grammie.**—Pain in sacral region; sweating at night, and heavy feeling across forehead on awakening next morning.

Highest temperature, 100·4° F. ten hours after.

December 15.—**Second injection, 0·003 grammie.**—Highest temperature, 101·6° F. ten hours after. Odynphagia so relieved that he *this day asked for meat, and ate with relish a plate of mutton.* (See p. 17.)



TEMPERATURE CHART OF H. H.—CASE 8.

N.B.—The shaded columns indicate the date and amount of the injection, each square representing one milligramme.

December 16.—Larynx more congested. Ulcers looking cleaner. Sputa less. Night perspiration less. Swallowing ‘capital.’ Urine loaded with urates.

December 17.—**Third injection, 0·004 grammē.**—Highest temperature, ten hours after, 102·6° F. A light bathing of pus over the cords at posterior part. The left arytenoid cartilage less swollen, and slightly more irregular at surface. Larynx less red, and free from pus. Infiltration less. Ulcers smoother and flatter. Very few bacilli in sputum.

Wakeful from cough at night.

December 18.—Weight, 8 st. 3½ lb.

December 19.—Temperature, 8 a.m., 98·8° F.; at 8 p.m., 101·8° F.

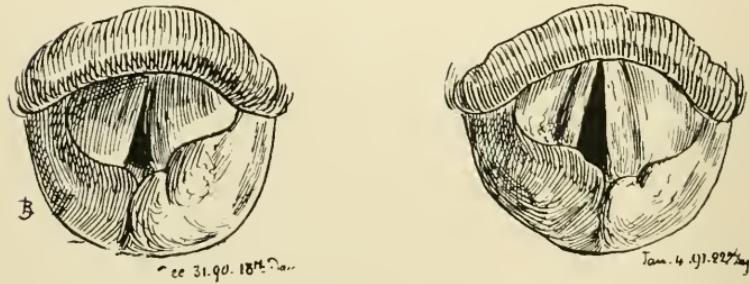
December 24.—**Fourth injection, 0·006 grammē.**—Highest temperature, 8 p.m., ten hours after, 102·8° F.; at 8 a.m. next morning, 99·6° F.

December 25.—Not so well; infiltration of right arytenoid of both ventricular bands and of epiglottis (Fig. XXVII.); swallowing very difficult, but not painful; breathing impeded.

December 26.—Very slight extension of dulness over *left* lung, with harsh expiratory sounds; here and there a few moist râles.

Also dulness over lower third of *right* lung, with harsh expiratory sounds. At night cough less troublesome.

December 27.—Swallowing still difficult. Temperature at midnight, 101·2° F.



FIGS. XXVII. AND XXVII*.

December 28.—Left lung improved, dulness of right lung extended. Laryngeal stenosis somewhat reduced, and ‘feels throat much better.’

December 29, 30, 31.—Swallowing again more difficult. No solid food since 25th. Cough very troublesome; physical signs unchanged.

January 1, 1891.—Marked improvement in breathing space and in swallowing; more cheerful; laryngoscope shows intense hyperæmia of epiglottis, but less thickening. The right aryepiglottic fold is much redder, and much more swollen than the left. (Fig. XXVII*.)

January 10, 1891.—The present condition of the patient is as follows :

The original infiltration of the **larynx** is less, and the induced infiltrations on the right side of the larynx and epiglottis are subsiding.

The natural shape of the epiglottis, which had been lost, is now clearly traceable, and there are one or two tuberculous nodules with light xanthoplasmic points.

The condition of the **lungs** is much the same, but **cough** is very troublesome.

The swallowing of fluids is easy when lying on his back, but he cannot take solids ; but there is perfect freedom from the pain which characterized the symptoms at commencement.

His maximum night temperature is 102° F.

Owing to the extreme prostration and the intensity of the symptoms, which are quite disproportionate to the physical signs, the injections have been discontinued.

Considering the protracted duration of the disease, and the man's habits, it is highly probable that the pulmonary changes are cirrhotic in their nature.

The unsatisfactory progress of the case is largely due to the circumstance that, although the physical evidences were favourable to injection, his constitution had become so undermined that the depressing power of the treatment was greater than the rallying power of the patient.

CASE 9.—Tuberculous infiltration and ulceration of larynx, with pulmonary disease (under Mr. Lennox Browne).

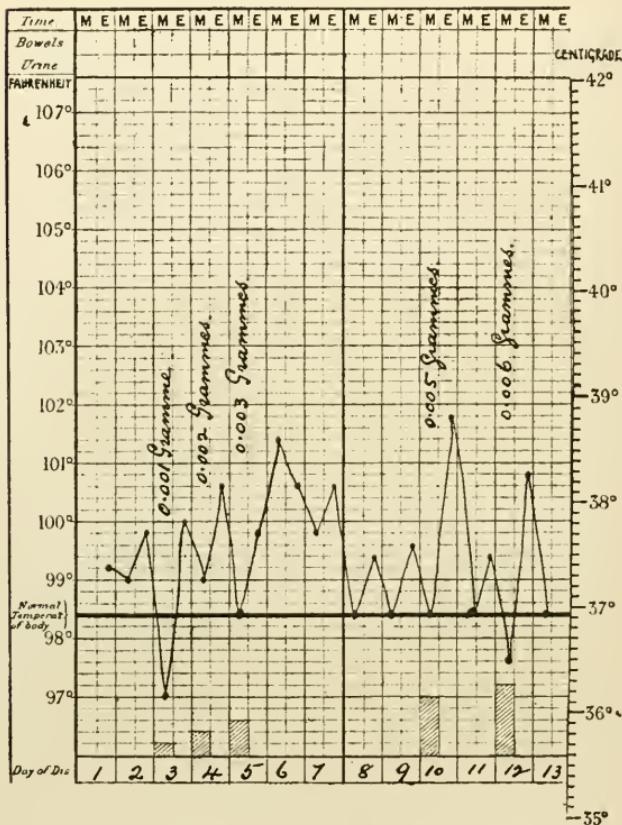
F. L., aged 35, admitted December 28, 1890, into the Central London Throat and Ear Hospital.

Family History.—Father died of asthma at 61. Mother died of old age at 68. Four brothers living.

Personal History.—Has had rheumatic gout at different ages.

Present Illness.—Has had a winter cough for five or six years, which has gradually commenced with increase of phlegm. Has had no lung diseases. Spat blood—dark colour and scanty—two years ago in the

spring. This was associated with a bad cold; did not lose his voice at the time. Eighteen months ago spat up about a pint after stooping down; it came up in mouthfuls; this also was not associated with voice change, but with cough. Three months ago brought up a pint of blood, not coughed up, but vomited, irrespective of cold, and after the exercise of a walk. This also was dark in colour.



TEMPERATURE CHART OF F. L.—CASE 9.

N.B.—The shaded columns indicate the date and amount of the injection, each square representing one milligramme.

Voice.—Was first affected twelve months ago, after taking cold; lost his voice, which gradually returned, and again disappeared. Voice has become gradually huskier and weaker since that event.

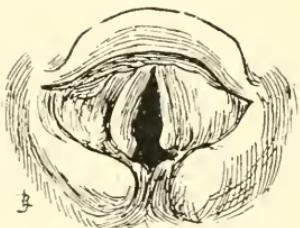
Deglutition.—Very painful for the last two months.

Nutrition.—Is thinner the last three months. No night-sweating till fourteen days ago; it is now only slight.

Larynx.—Infiltration of both arytenoids, especially of the left. Similar swelling of aryepiglottic and glosso-epiglottic fold; some thickening and ulceration of under surface of epiglottis, and of ventricular band. Both cords thickened, and swollen at the vocal process. Ulceration of the left cord at this situation. (Fig. XXVIII.)

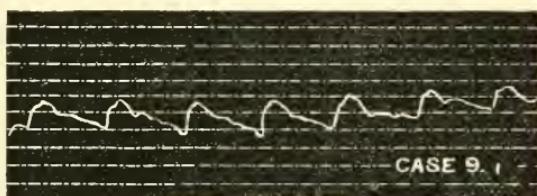
Chest.—Slightly diminished resonance on percussion on *right* supra and infra-clavicular region; marked dulness over *left* supra and infra-clavicular region. Diminished expansion on both sides, especially left. Some harsh breathing over both apices, especially left, where a few râles are heard.

Heart-sounds accentuated.



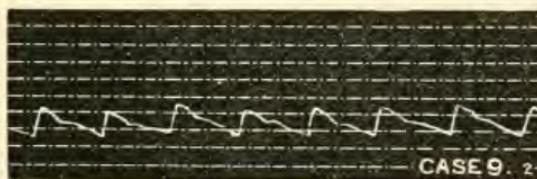
F.L Dec. 24. 90

FIG. XXVIII.



Pulse-tracing—1. Before Injection.

Temp. 98·8° F.; Pulse 90; Resp. 18.



Pulse-tracing—2. During Reaction.

Temp. 100·8° F.; Pulse 92; Resp. 36.

December 31.—First injection, 0·001 grammes. Highest temperature, ten hours afterwards, 100° F. Pulse 99. Respiration, 22.

January 1.—Swallowing distinctly improved. Second injection, 0·002 grammes. Highest temperature, six hours after injection, 100·6° F. Pulse, 80. Respiration, 20. Four hours later: Temperature, 99·8° F. Pulse, 100. Respiration, 32. Suffered much from cough at night; pain in the back, heat, but no perspiration.

January 2.—Third injection, 0·003 grammes. Ten hours afterwards: Temperature, 99·8° F. Pulse, 104. Respiration, 34. Eighteen hours

afterwards : Temperature, $101\cdot4^{\circ}$ F. Pulse, 98. Respiration, 43. Complained of increased soreness in throat, but improvement in deglutition.

January 3.—Evening temperature, $100\cdot6^{\circ}$ F.

January 4.—,, , $100\cdot6^{\circ}$ F.

January 5.—,, , $99\cdot4^{\circ}$ F. Can swallow better.

January 6.—,, , $99\cdot6^{\circ}$ F. Well-marked harsh breathing with râles, and pectoriloquy heard two inches below left clavicle.

January 7.—Morning temperature, 98° F. Pulse, 74. Respiration, 20. **Fourth injection, 0·005 grammme.**

January 8.—Night temperature, $97\cdot6^{\circ}$ F.

January 9.—**Fifth injection, 0·006 grammme.**—Highest temperature, $100\cdot8^{\circ}$ F., ten hours after.

January 10.—Larynx looking much cleaner, and less swollen. Feels better in every way. Morning temperature, normal.

CASE 10.—*Laryngeal tuberculosis associated with pneumonia.*

Further development of the disease under injection. General improvement (under Professor Gerhardt).

R. H., aged 45, a stonemason's labourer, admitted September 17, with a history that he had been ill since February, 1889, but had become worse in the last few days, the cause of which exacerbation was found to be acute pneumonia at the left base. His voice was also hoarse. This was due to a swelling on the right vocal cord of the dimensions of half a lentil. The mucous membrane was generally congested, and the inter-arytenoid fold was uneven. The pneumonia subsided under treatment, but, there being numerous tubercle bacilli in the sputa, he was injected with 0·002 grammme on November 17. There was no reactionary fever, even on a repetition of 0·005 grammme, and only slight reaction on administration of 0·01 grammie; but after the first injection a dulness not previously existing was discovered at the right apex. It was not until after the tenth injection, when 0·05 grammie was employed, that laryngeal changes had become very marked. When I saw him, on December 5, there were, beyond the usual general infiltration of the aryepiglottic folds of the mucosa over the arytenoid cartilages and of the inter-arytenoid fold, great inflammatory swelling of the left ventricular band, and a small ulcer on the right true cord, in the position of the vocal process. His condition was stated to be better than it was a few days previously.

In this case, one of the earliest submitted to treatment, the general state had greatly improved. The expectoration, which formerly contained blood and pus, was now almost purely of mucous character, and was markedly less. The bacilli were also perceptibly fewer—though, of course, the prognostic value of this circumstance is open to dispute. Cough was almost gone, and weight had been gained.

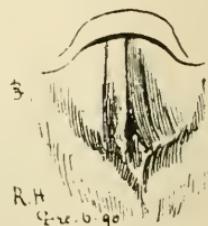


FIG. XXIX.

CASE 11.—Acute tuberculosis of the larynx. Tracheotomy before injections. Further development of the infiltration under treatment (under Professor Gerhardt).

M. M., female, aged 23, admitted into the Charité Hospital, on November 23, on account of acute stenosis of the larynx, for which it was necessary to at once perform tracheotomy. She had only been delivered in childbirth three days previously. Three injections had been made between November 30 and December 4, commencing with 0.001 grammie, and increasing a milligramme with each successive dose. So far the stenosis had been increased, but otherwise there had been but little local reaction. In the chest there was observed infiltration at the right apex, and tubercle bacilli were present in the sputa. When I saw her on December 5 there was the appearance on the epiglottis pointing to probable release of necrotic tissue.

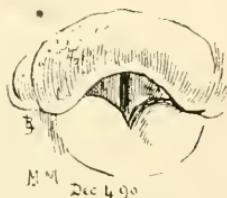


FIG. XXX.

CASE 12.—Tuberculosis of pharynx, larynx, and lungs. Odynophagia. Development and improvement under treatment (under Professor Gerhardt).

W. S., aged 41, a tradesman, was admitted into the Charité Hospital on November 10. In the lungs there was only to be discovered very slight dulness at the right apex, which might have been due to the presence of greatly swollen



FIG. XXXI.

glands in the supra-clavicular space. The whole chain of cervical glands on each side of the throat were greatly enlarged. The patient complained of extreme pain in swallowing, and on examination of the throat it was seen that both tonsils and uvula were enlarged and inflamed, and that the surface of the left tonsil

and fauces was covered with yellow spots diagnosed as tuberculous. Other similar spots, fewer in number, were seen on the uvula, and one patch on the right tonsil. The epiglottis and larynx generally were much infiltrated. Tubercle bacilli were found. The first injection of 0·002 grammie was made on November 17, and since that date six others had been made, the last amounting to 0·01 grammie. After commencement of the injections the glands in the neck became larger, and, after the sixth, probably as an attempt to throw off necrotic matter, a large perforating ulcer was observed in the left tonsil. Had not one known the nature of the case from other sources, and of the changes that take place under Koch's treatment, one would have at first sight diagnosed this ulcer, from its naked-eye appearances, as due to syphilitic or to some intensely insanitary origin. Great relief was afforded to the odynphagia, so that the patient refused to be bothered with applications of cocaine before food-taking.

**CASE 13.—Long standing. Tuberculosis of larynx and lungs.
Slow reaction, without improvement (under Professor Gerhardt).**

A. H., aged 47, an upholsterer, was admitted into the Charité Hospital, on November 11, suffering from cough and expectoration for six months, with hoarseness for eight weeks. Tubercle bacilli were present in the sputa, and infiltration was detected at both apices of the lungs. In the larynx there was seen to be very considerable stenosis, due to enormous infiltration of the left ventricular band; the aryepiglottic folds were also much infiltrated. The right cord only was visible. It was much inflamed, and was situated considerably to the right of the middle line, but there was no external glandular or other external tumour to account for this displacement. The first injection of 0·001 grammie was made on November 22, and the seventh and last, of 0·008 grammie, on December 5. Reactionary fever had only been observed after the last two, and although the glottic swelling had become somewhat increased, and the colour had changed, the laryngeal condition was practically the same. In the last day or two one or two yellow points, indicating necrotic changes, had been observed.

**CASE 14.—Slight pulmonary and laryngeal tuberculosis. Development under treatment of ulcers on the vocal cords.
Complete healing within a week (under Professor Gerhardt).**

L., single, female, aged 21, when admitted was suffering from but very slight pulmonary disease, there being only perceptible a dulness at the left apex, which was not to everyone appreciable. After the first injection this dulness in the lung became quite marked, and in the larynx a very interesting phenomenon was exhibited. Prior to treatment the only laryngeal lesion was a swelling with slight

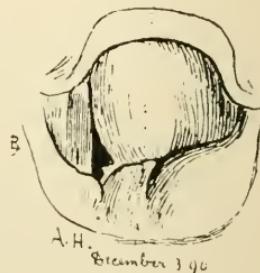


FIG. XXXII.

ulceration of the posterior wall. After injection of 0.002 grammes on November 26 there were observed not only some general increase of hyperæmia of more than usually high grade extending down the trachea—and this still existed when I saw her on December 4—but two symmetrical ulcers on the edges of the vocal cords, which themselves were highly injected. These ulcers commenced posteriorly just in front of the vocal process, and extended almost to the anterior commissure. At



FIGS. XXXIII. AND XXXIV.

first they were white, but on the second day of their existence were observed to be yellow, as if covered with a thin layer of 'laudable' pus—a condition to which Professor Gerhardt has given the term 'Xanthoplasma.' They had been noted as undergoing healing on December 2, and when I examined the larynx they were actually healed, their former site being marked only by some slight pallor, and a want of the normal glistening appearance of the cords, which were otherwise still unduly red, especially the right. The ulcer on the posterior wall, and the thickening, had also partaken of the reparative process. In this girl was also to be observed the remains of one of the various exanthems which have been noted to follow injection as a toxic symptom. The rash in this case appeared on the abdomen and back, and, commencing as a rosy red, speedily became brownish, and then resembled the ordinary skin eruption common to secondary syphilis.

CASE 15.—*Laryngeal tuberculosis, with slight pulmonary disease.*

Hæmoptysis and increase of subglottic infiltration under treatment (under Professor Gerhardt).

H., female, aged 38, admitted with small limited area of dulness at the posterior part of the lung between the spine of the scapula and vertebral column. The first injection, on November 29, of 0.002 grammes, was followed by hæmoptysis, a result that has occurred in only one other of the forty cases already under Professor Gerhardt; but there was no repetition after a subsequent injection of a like quantity. In the larynx there was observed general infiltration of the mucosa of the posterior wall, which was of a high red colour, brighter than normal; there was also ill-defined and slight subglottic infiltration of the left cord. After treatment this infiltration became much more pronounced; generally the contour of the posterior wall of the larynx was ill-defined, but there was a well-marked difference on the right side, in the shape of a swelling on the under

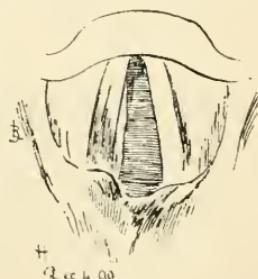


FIG. XXXV.

surface of the right cord. When I saw her (December 4) this swelling had also increased, and a red prominence of the cartilage adjacent to the affected cord was observed. On a second examination (December 5) this had already disappeared. In this case there was evidently perichondritis of the right arytenoid cartilage.

CASE 16.—Laryngeal tuberculosis, causing dysphagia, with disease of right lung. Development and absorption of quasi-new growth in larynx under treatment (under Professor Gerhardt).

K. W., aged 38, was admitted November 11 into the Charité with dysphagia, cough, expectoration, and dyspnoea. No cavity was to be discovered, but there was dulness at the right apex; the sputa were nummulated, and contained bacilli. The first injection of 0·001 gramme was made on November 28, and had been repeated three times to the amount of 0·005 gramme. Dysphagia had increased after the first injection, and at the date of my examination, December 5, there existed enormous swelling of the coverings of the arytenoids, especially the left. There was a distinct tuberculous outgrowth in the posterior commissure, which in the last twenty-four hours had become ulcerated, and was evidently undergoing necrotic change, and would probably be altogether thrown off. There were also large ulcers on both vocal cords, which were themselves inflamed and thickened. In the last twenty-four hours there had been observed oedema of the uvula; this signified either intensity of the toxæmia, or the presence of tubercle in that situation. Examination on December 9 showed that the quasi-growth was undergoing resorption.

CASE 17.—Acute pulmonary and laryngeal tuberculosis, intense odynophagia. Exacerbation of pain and subsequent alleviation under treatment. Death; autopsy (under Professor Krause).

G., married, aged 24, admitted suffering from intense dysphagia, due to enormous infiltration of the epiglottis. This somewhat increased, and was followed by ulceration, with no alleviation of suffering after the first injection of 0·001 gramme on November 24. The patient was so debilitated that treatment was remitted. When I first saw her the epiglottis was acutely swollen and ulcerated, as were also the pharyngo- and laryngo- epiglottic ligaments; but in two days much was changed for the better; the oedema was reduced, and a healing process had evidently commenced. The patient was able to take soup almost without pain. Nevertheless, the extensive pulmonary disease in this case, and an aggravated general cachexia, precluded the possibility of any but a most unfavourable prognosis. This patient died during my visit, and the autopsy revealed destruction of the upper half of one lung, with attempts, however, at active repair in one or two spots. There was also general ulceration of the larynx, with several spots of cicatrization.

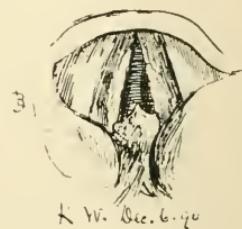


FIG. XXXVI.

CASE 18.—*Pulmonary and laryngeal tuberculosis. Great odynophagia, which was relieved under treatment (under Professor Krause).*

A. S., aged 42, railway servant, admitted with infiltration of upper third of left lung, had great pain and difficulty of swallowing, due to laryngo-pharyngeal swelling and ulceration, as noted in the accompanying drawing. Under treatment, expectoration diminished in quantity and improved in character. In the last few days swallowing had greatly improved, and the patient reported with gusto that he could now drink beer, which he had not been able to do for many weeks.

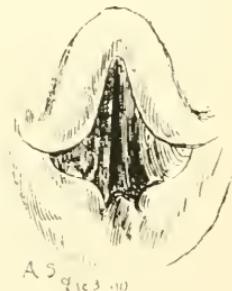


FIG. XXXVII.

CASE 19.—*Laryngeal tuberculosis. Great improvement under treatment (under Professor Krause).*

S., male, aged 21, applied on account of hoarseness, pain and cough. There was observed an ulceration with elevated edges on the posterior wall of the larynx, which was itself greatly infiltrated. This had gradually improved under treatment, first by a lowering of the edges of the ulcer, which had then healed, and, finally, by a gradual absorption of the infiltration. This I observed at my first visit on December 1, and I witnessed further marked improvement at two subsequent visits. Lately, a little yellow prominence pointing to necrotic change had been observed over the right arytenoid cartilage, and a small ulcer at the vocal process of the corresponding vocal cord. In this case eleven injections had been employed in a space of seventeen days, commencing with 0.001 and amounting gradually to 0.02 grammes.

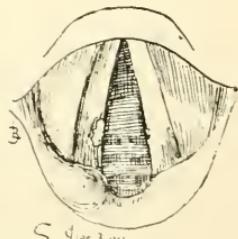


FIG. XXXVIII.

In connection with the improvement in this case, Professor Krause mentioned that of a brother medical practitioner, in which under treatment a tuberculous thickening of the inter-arytenoid fold had entirely disappeared.

CASE 20.—*Laryngeal tuberculosis with extensive pulmonary disease. Improvement of larynx under treatment (under Professor Krause).*

F., aged 26, applying on account of loss of voice, with cough, in the sputa of which bacilli were found, was treated by ten injections of from 0.001 grammes

to 0·04 grammie between November 13 and December 3. At the commencement of treatment, the cords were somewhat congested, and there was slight inter-arytenoid infiltration. There was also extensive disease of the left lung. After the first injection, there was observed an exfoliation at the right vocal process, and an appearance as of extravasated blood around the posterior portion of that cord. Later, ulcers appeared on the cartilaginous portions of both cords. Between December 3 and December 5 I observed that these ulcers were rapidly healing, and this in spite of the extensive pulmonary mischief.

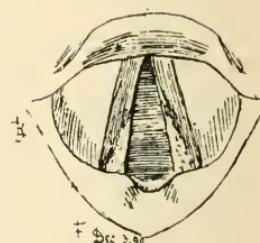
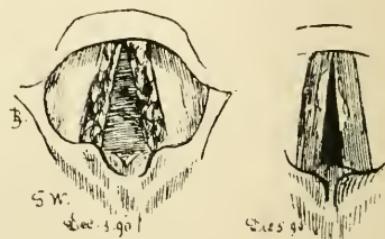


FIG. XXXIX.

CASE 21.—Tuberculosis of lungs, with hyperæmia on the vocal cords. Development and healing of ulcers under treatment (under Professor Krause).

G. W., aged 33, a clerk, with extensive infiltration of both lungs. Had thickening with great hyperæmia of both vocal cords, but without ulceration. The malady had commenced in April, as a sequel of influenza, and the patient applied on account of hoarseness and cough. After injection the hyperæmia of the cords was intensified and covered by numerous raised ulcerating points. This I saw on December 3, it having then existed only one day. On December 5, only two days later, the cords were already smooth and with only two superficial and nearly symmetrical ulcers at their free edges. The surface of the cords was observed to greatly resemble that of the glazed skin of patients suffering from lupus after removal of the crusts consequent on these injections. The injections in this case had already been seven, and varied in quantity from 0·001 to 0·01 grammie. On December 3 the eighth was employed, to the amount of 0·02 grammie. With regard to the somewhat large dose here employed (a circumstance also to be noted in Case 9, 17 and 19), before there was any great reaction the Professor mentioned that in one case in his private practice he had employed as much as 0·04 grammie, without any reaction, although the diagnosis was fully established by the presence of numerous bacilli in the sputum.



FIGS. XL. AND XLI.

CASE 22.—Pulmonary tuberculosis, with catarrh of the larynx, quickly developing into typical tuberculosis on injection (under Professor Gerhardt).

A. F., aged 24, a tailor, admitted into the Charité Hospital on November 23, with infiltration at the right apex of some standing, and hoarseness and some pain

in the throat of only a day or two. These latter symptoms were thought to be due to a slight catarrh, but after injection of 0·002 grammie on November 29, not only did the previous slight congestion greatly increase, but there developed the characteristic thickening of the posterior wall, as figured in Case 7. With further injections—the last amounting to 0·01 grammie—expectoration had much diminished and become more mucous in character; also the number and character of the bacilli had given evidence of improvement in the lung affection.

CASE 23.—Pulmonary tuberculosis, with tubercular infiltration in larynx. Development of ulceration on first injection (under Professor Gerhardt).

M., 28, married, and *enceinte* five months, admitted with well-marked disease in left lung. In the larynx were observed slight redness and thickening of the posterior wall, with that general loss of contour of the aryepiglottic folds, and of the prominences of the cartilages, which is so characteristic of tuberculous infiltration of the larynx in the pre-ulcerative stage. After the first injection of 0·001 grammie on December 3, there was observed a roughness on the posterior wall, and some increase of redness. This was the condition when I saw her on December 4, and in addition several of the glandules of the epiglottis were notably more prominent than usual. It appeared possible that these might be points of commencing ulceration, but on the next day they were no longer visible.

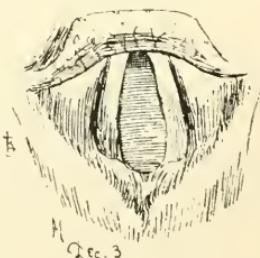


FIG. XLII.

CASE 24.—Double pulmonary tuberculosis and tubercular infiltration of larynx. Subsidence of laryngeal evidences under injections (under Professor Gerhardt).

E., female, aged 38, married, admitted with extensive tubercular disease of both lungs. In the larynx were to be observed characteristic pallor and swelling of the inter-arytenoid fold and posterior commissure of the larynx. There was no increase of swelling, and hardly perceptible difference in colour after the first injection, but under further treatment the morbid thickening had greatly diminished. In this case the first injection had been made on November 21, and had been repeated six times, seven injections in all, commencing with 0·002 grammie, and increasing to 0·02 grammie.

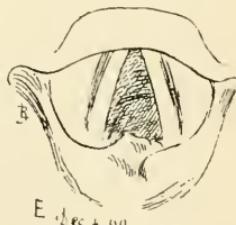


FIG. XLIII.

CLASS III.

CASE 25.—*Slight evidences of pulmonary and laryngeal tuberculosis. Injections for diagnostic purposes. Satisfactory result (under Mr. Lennox Browne).*

A. B., aged 18, admitted, December 14, into the Central London Throat and Ear Hospital, and transferred to me by courtesy of Mr. Jakins.

Family History.—Father living, but suffers with haemoptysis. Mother living, and healthy. Two brothers died of phthisis. Three living, and healthy. Also four sisters living, and healthy.

Personal History.—No illness, excepting haemoptysis last February and May. On the first occasion, the amount of blood measured half a pint; but there was much less on the second occasion. Has no cough or other pulmonary signs. Voice unaffected. No dysphagia. At first lost weight, but lately has slightly regained it. Appetite always good. Occasional night-sweats.

Present State.—**Right Lung:** Breathing somewhat harsh over upper lobe. Expiration prolonged and audible. Vocal resonance and percussion somewhat dull. No râles. Expansion good. **Left Lung:** Normal. No bacilli. Weight, 8 st. 12 lb.

The chief features of the injections, which were commenced on December 14 with 0·002 milligrammes, and increased daily to a centigramme, were: First, that there was never a rise in temperature more than one degree; there was little or no pain, dyspnœa, or cough; no rash; and the only evidence at all of reaction was a marked increase in urates. The **Larynx**, which had shown slight thickening at posterior commissure, and some general hyperæmia prior to injections, evidenced no change, except perhaps for the better after the first three days. In the **Lungs** there was no variation whatever.

At the end of a week 0·015 gramme was administered; and this failing to produce any increased reaction, the patient was discharged, and recommended a sea-voyage.

CASE 26.—*Doubtful diagnosis of lupus of the ear confirmed by Koch injections (under Mr. Lennox Browne).*

ELIZABETH H., aged 51, admitted into the Central London Throat and Ear Hospital, December 13, 1890.

Family and Personal History.—Good. Has had a large family of twelve children, all of whom were born alive, and eight are still living. Still

menstruating. Has been treated successfully for lupus of the face by Unna's plaster, and has several small scars on the cheek and nose.

Present State.—She is now suffering from a somewhat painful inflammatory infiltration of the lobe of the ear, which presents an appearance very similar to that of the haematoma of the insane, and such as I have once or twice witnessed as the result of accident. Not only is the whole pinna much swollen and oedematous, so that none of the fossæ or prominences are to be made out, but it is of a dull purple hue. Tense and very brawny to the touch. It is $2\frac{1}{2}$ inches in length—more than $\frac{1}{4}$ inch longer than the right, and of corresponding increase in breadth. There is rather offensive ichorous discharge from the meatus, itself much narrowed by the swelling, and from behind the ear, where Mr. Jakins had made an opening on account of symptoms pointing to an abscess from this spot, there had been discharges of similar character to that from the meatus. This patient had been for some time an out-patient, under treatment by iodide of potassium, biniodide of mercury and other remedies, to all of which there had been no response, and it became a question whether the nature of the case might not be malignant. But with a view of testing the possibility of it being a fresh development of the tuberculous dyscrasia which had given rise to the former lupus ulcer on the face, it was determined to submit the patient to some Koch injections.

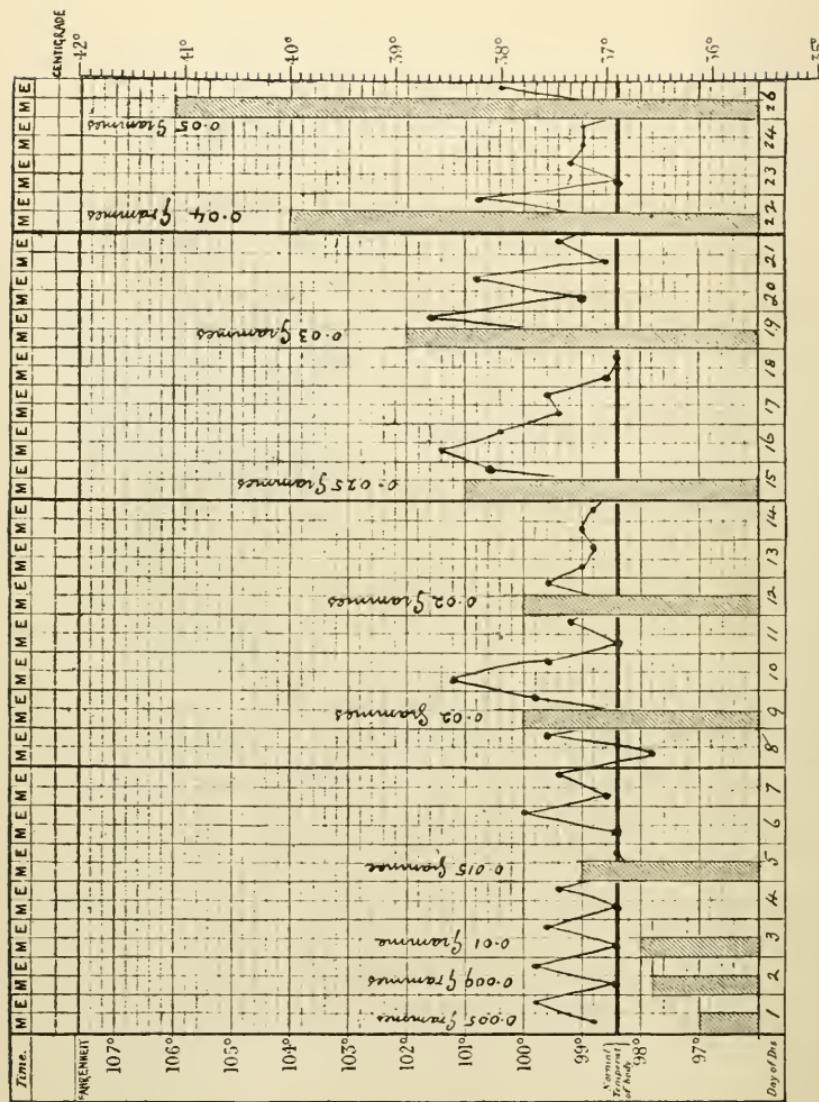
December 16, 1890.—First injection of 0.005 grammie.—General reaction but slight; but ear rather more painful four hours afterwards.

December 17.—Second injection, 0.01 grammie.—General reaction still slight. Abundant discharge of urates, aching in limbs, and nausea. Increase of pain, and swelling in the ear.

December 18.—Third injection, 0.01 grammie.—Reaction, as tested by temperature, and pulse still very moderate; but continuance of other symptoms.



FIG. XLIV.
(Life-size.)



TEMPERATURE CHART OF E. H.=CASE 26.

N.N.B.—The shaded columns indicate the date and amount of the injection, each square representing one milligramme.

December 19.—Catamenia appeared.

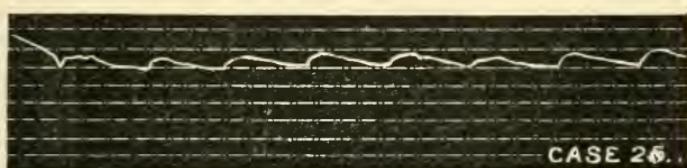
December 20.—Fourth injection, 0·015 grammie.—No increase in reaction.

December 21.—Rise of temperature to 100° F. without further injection.
Increase of aching in limbs, and of pain in the ear.

December 24.—Fifth injection, 0·02 grammie.—Very slight reaction till midnight, when temperature rose to 101° F. Discharge from ear less, both in quantity and in offensiveness.

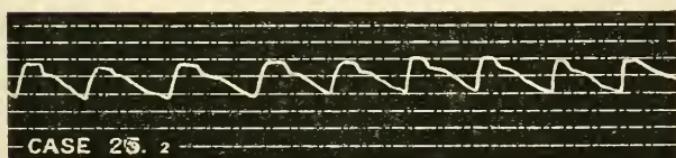
December 25.—Temperature at 4 and 8 p.m. 100·6° F.

December 27.—Sixth injection, 0·02 grammie.—Hardly any reaction.



Pulse-tracing before Injection.

Temp. 99·4° F.; Pulse 72; Resp. 18.



Pulse-tracing during Reaction.

Temp. 100·4° F.; Pulse 80; Resp. 24.

December 30.—Seventh injection, 0·025 grammie.—Ear very painful, and skin around flushed. Temperature at midnight 101·4° F.

January 3, 1891.—Eighth injection, 0·03 grammie.—The same temperature reaction as on last occasion, the rise recurring at the same time on the next day.

January 6.—Ninth injection, 0·04 grammie.—Highest temperature, 100·8° F.

January 7.—Tenth injection, 0·05 grammie.—Highest temperature, 100·4° F.

A careful examination shows that the ear is much softer, much less infiltrated, and hardly at all painful. The colour is changed from a dusky purple to a tint only slightly in excess of the normal. Scales have continually formed over

the infiltrated parts, and have desquamated ; and now not only is the discharge less, but the opening posteriorly is closed, and the natural meatus is becoming more pervious on subsidence of the surrounding œdema. The markings of the helix concha, etc., are each day more distinguishable. The exceedingly slight general reaction, and the gradual character of the local changes, give the best assurance of an ultimate cure.

CASE 27.—Suspected tuberculosis confirmed by injections (under Professor Gerhardt).

T., female, aged 31, in whom there was to be found neither dulness of the lung nor bacilli, there being no sputa, and the only evidence of tubercle was an attack of haemoptysis. There was no reaction till after the menstrual period, and until administration of the axilla injection, which consisted of 0·02 gramme, the first having been 0·002 gramme. After this sixth injection moist râles were heard, with expectorations which contained bacilli, and slight but perceptible dulness could be detected in the upper part of the right lung.

CASE 28.—Presumed confirmation of cure of tuberculosis by absence of reaction after repeated injections (under Professor Krause).

G., male, aged 46, an engine-driver and a big, powerful man, came under this treatment on November 30, with but very slight disease of the lungs, and such scanty expectoration that all attempts at search for bacilli were futile. In the previous July, however, a small ulcer, situated at the extreme posterior aspect of the left vocal cord, had been curetted out, and under microscopic examination had revealed infiltration of the epithelium and well-marked giant cells. A similar procedure in the same spot was repeated in September, when in addition there were to be seen evidences of tubercle undergoing caseous degeneration. These preparations I had the pleasure of seeing. The laryngeal appearance, which consisted of soft fleshy thickening of the left cord, with some loss of contour, and inter-arytenoid swelling, was by no means certain evidence of tubercle, nor was there the least reaction even after the third injection, which amounted to 0·008 gramme. On December 5, 0·01 gramme was administered. This was increased on alternate days up to the extent of 0·04 gramme, and the case was set down, not unfairly, as one of cure by the lactic acid treatment formerly employed.

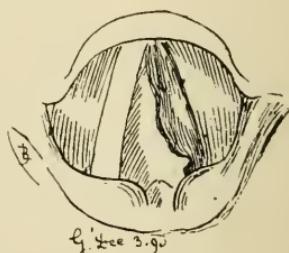


FIG. XLV.

CASE 29.—Confirmation of diagnosis of syphilis by negative result of injections (under Professor Krause).

T., aged 29, was suffering from pulmonary disease, with bacilli in the sputa, but with no affection of the larynx. On the posterior wall of the pharynx there existed a punched-out ulcer with red and angry elevated edges. The patient admitted a primary chancre ten years previously. No local reaction had been observed after repeated injections, even to the extent of 0·009 grammie. Professor Krause asking me, I expressed my opinion that the ulcer was highly characteristic of tertiary syphilis. In this he also agreed, though he stated that his view was opposed by all three of his very able assistants, who based their conviction of a contrary diagnosis on the presence of bacilli in large numbers, and on the fact that, with improved methods of examination, the combined presence of syphilis and tuberculosis is found to be more and more rare in occurrence.

CASE 30.—Diagnostic injection for enlarged cervical glands.

Verification of tuberculous nature by prompt reaction and speedy promise of improvement (under Mr. Lennox Browne).

H. B., aged 17, first seen January 5.

Previous History.—Delicate from birth. Scarlet fever eleven years ago.

Is a mouth-breather. Snores loudly, but much more so the last three or four months, during which he has been feeling very ill, with varying, but on the whole increasing, enlargement of the glands of the neck. Has suffered from cough without much expectoration, and is thinner.

Family History.—Father died at 38 ‘of epilepsy.’ Mother living, healthy.

Two brothers and one sister living; three died in infancy. Father’s brother died of phthisis.

Present Condition.—The cervical glands from the ear to the clavicle—where there is a swelling the size of a hen’s egg—are very enlarged and painful, very sensitive to the touch, and looking as if about to ‘point.’ The **throat** and **larynx** are both somewhat inflamed. Dulness on percussion is found over the lower third of the left lung, with harshness and prolongation of breath-sounds over the same area. Tubercle bacilli not discovered. Urine normal. Slight diarrhoea. Rather excessive perspiration. Temperature normal.

January 11, 1891.—First injection at 11 a.m. of 0·001 grammie. Six p.m.: Temperature, 99·6° F. Pulse, 72. Respiration, 20. Pain in the back.

January 12, 2 a.m.—Temperature, 100·4° F. Chest rather oppressed and breathing laboured. Slight headache all day. Six p.m.: Temperature, 100·6° F. From this time the temperature declined, and

January 13, at noon, it was only 98·6° F. His **neck** is hardly at all painful when touched, and without pain otherwise. The swelling is perceptibly reduced. The **lung** is much more resonant, and gives evidence of much freer entry of air.

January 15.—Second injection, 0·003 grammie. Highest temperature, 103° F., with renewal of all former symptoms of reaction, but increased relief on their subsidence.

CASE 31.—*Injections for ascertaining extent of lung mischief, and character of laryngeal hyperæmia. Satisfactory result, and improvement on continuance of treatment* (under the care of Professor Gerhardt and Mr. Lennox Browne).

Mr. ——, aged 47, an engineer, consulted me, on the recommendation of Dr. Service, of Bilbao, in June, 1890, on account of slight morning haemorrhages, which occurred immediately on waking, and sometimes appeared to have accumulated in the throat during sleep. This had followed on an attack of epidemic influenza earlier in the year.

His *previous history* was interesting. The last twenty-eight years had been spent mainly abroad—Spain, Sardinia, the Caucasus, Brazil, Peru, had been residences of from two to four years' duration; but the last ten years he had been at Bilbao, in Spain, where the climate is generally damp and changeable, and the town boasting one of the highest death-rates in Spain—namely, 41 per 1,000—the causes of death being chiefly diseases of infancy and phthisis. The town is built in a narrow *cul-de-sac*, surrounded on three sides by hills; a river (very insanitary) runs through the centre of it to the Bay of Biscay, on the shores of which (at Santurce) the patient lived. The scene of his labours was at some quarries, situated eight miles inland, on an elevation of 1,000 to 1,500 feet above the river-level.

Previous illnesses had included a long and very enfeebling attack of remittent fever in Peru, in 1879, with thrombosis in the left leg during convalescence, and a fistula, believed to have originated at the same time, and for which he was successfully operated on in August, 1888.

His parental history was good, and all his children—one son (19) and two daughters—were in good health. He had always been rather delicate in appearance, and very thin; but he had done much work, and in the summer previous to the attack of influenza he had taken a walking tour of three weeks in Lapland.

When I first saw him in May, his lungs were healthy, and his symptoms were thought to be due to intense varix of his throat, for which I applied the galvanocautery. As a result, all haemorrhage stopped; but on returning to Bilbao he had much fatigue and extra use of the voice, due to a strike amongst his miners, etc. As a consequence, he had a relapse of his trouble, and he returned to me on November 3, when I was much struck with the change in his appearance. He was much thinner, having lost 4 lb. in the last week, and was suffering from distressing cough with muco-purulent nummular sputa, occasionally haemorrhagic, which contrasted strongly with the ‘anchovy-paste’-like mass which used to arise each morning. To quote his own words, in a letter, written on November 5, after the undernamed consultation: ‘The largely-increased quantity of expectoration commenced on Sunday, November 2, on the journey from Bilbao to London,

gradually increasing for two days, and now (November 6) apparently stationary. With all deference, I venture to think that I have caught a cold on the journey, and that *this* expectoration is really not proceeding from the same place as that which I formerly had mixed with blood, because I could feel that *trickling* down very often, and I expectorated *without effort*, whereas now I have to cough it up.' This suggestion is probably correct, for the recent bleeding stopped in a day or two, and then fitfully recurred. There was no history of night-sweats.

On examining the patient, the **throat and larynx** were seen to be intensely hyperæmic, but with no evidence at all characteristic of tubercle.

On November 5, I had the advantage of a consultation with Dr. Dawson Williams, who gave the following report of the *physical examination* of the chest :

' Movements equal. Percussion note in left sub-clavicular region slightly high-pitched. On auscultation, respiration harsh, expiration prolonged and wavy. At the end of inspiration, a few distant, medium-sized mucous râles. No moist sounds or deficient resonance elsewhere.'

Later, on December 2, Professor Gerhardt detected a very slight bruit on expiration at the extreme apex, and diagnosed an aneurism of a minute branch of the pulmonary artery passing through a very small cavity.

Bacilli (not very numerous) and a few elastic fibres were found in the sputa by Mr. Wyatt Wingrave on one occasion, but not subsequently. Urine, normal. Evening temperature, 101° F. Morning, 100° F.

Dr. Dawson Williams, on a second consultation, agreed with me that he was a good case for treatment by injections of Koch's fluid, especially with a view of ascertaining the limits of the tuberculous process, for it was difficult to believe that so small an amount of disease was sufficient to account for the extreme prostration and emaciation from which he was suffering.

Accordingly I went with the patient to Berlin, and he was submitted to Koch's treatment by Dr. Carl von Noorden, and later, in consequence of the illness of this gentleman, by Staff-surgeon Dr. Hertel, under the supervision and occasional observation of Professor Gerhardt.

Twenty-four injections were made in all, commencing on December 1, 1890, with a milligramme, which, after a centigramme had been reached, was raised gradually to a decigramme—this last full dose being repeated on two occasions. Reaction was very moderate till a centigramme was reached, the highest temperature being only 102° F. After the fourteenth injection there was a slight haemoptysis, which did not recur. After a centigramme the dose was raised to a decigramme (*January 3, 1891*), which gave a reactionary temperature of 101° F.; but the highest temperature was registered after the second dose (*January 11, 1891*) of this quantity, when it rose to 103·3° F.

The patient is to receive one or two more doses of a decigramme, and is then to go to Egypt for the rest of the winter. He has suffered hardly at all from the severe winter during his seven weeks' residence in Berlin, has never been confined to bed, and has frequently gone out walking or driving. His cough and expectoration are better, and he has gained 4 lb. in weight since the commencement of the treatment.

A report of his lungs, on December 30, by Dr. Hertel, stated that the throat was much as it has been all along—no reaction—thus confirming the first diagnosis that the larynx was free from tubercle. There was decided improvement in the chest, the area of disease being much smaller, and the cavity showing signs of closing.

On January 11, Dr. Von Noorden returned, and confirmed this opinion ; but I have not yet received Professor Gerhardt's final report.

This case must be taken to be equally satisfactory from the double point of view of the diagnostic as well as the remedial effect of the injections.

Summary.—Not to be analytical to the extent of weariness, there are certain circumstances of interest which are specially worthy of note in each of the three classes of the reported cases, and in each variety of tuberculosis treated.

Lupus.—The cases under this heading were **six** in all. We find that in three instances of **external lupus**—Cases 1, 2, and 5—there has been a development of the same disease in the uvula ; in one (Case 1), absolute changes of the nature of lupus, but to the eye not distinguishable from those of tuberculosis, in both the larynx and the trachea, and also in this case a development of pulmonary disease not previously noted. This last phenomenon is well described in the paper of Dr. Von Noorden, to which allusion has already been made. In two other cases of lupus (5 and 6) there was long-standing evidence of the disease in both the fauces and the larynx, and these were both re-awakened as the result of the treatment. In only one (25) out of six cases of lupus was there not a manifestation of the disease in some part of the throat either before or as a result of the injections. To finish with this disease, in every one there has been such a measure of improvement as to carry conviction of an ultimate cure.

Tubercular Laryngitis.—Of this disease we have **twenty**

examples. In one case (3) laryngeal evidences were developed after injection for a pulmonary disease; in another (4), faacial tuberculosis arose anew as a secondary effect of the treatment for a laryngeal infiltration.

In one case (12) there was from the first tuberculous disease in both the pharynx and the larynx. In two other cases (21 and 22) a laryngeal catarrh, associated with pulmonary tuberculosis, quickly developed typical evidences of tubercular laryngitis. In almost every case of already existing tubercular laryngitis, it will have been observed that there was a development of latent disease in situations other than those for which the treatment was commenced.

As to **stenosis**, there was narrowing of severe grade prior to the injections in two cases (11 and 13), and in one (8) as a result of treatment. Tracheotomy had been performed in one (No. 11) before injections, and was not necessary in either of the others.

Ulcerations developed or extended in a considerable number of the cases in which there had been previously only hyperæmia and tumefaction, or only small points of erosion.

Improvement of ulcers may also be noted in many, while actual **healing** took place in five (14, 19, 20, 21, and 24), as well as in another under Professor Krause not enumerated (p. 95).

Dysphagia, or **Odynphagia**, was present in four cases (8, 12, 16, and 17), and in three (8, 12, and 17) marked relief of the suffering occurred as a sequence of the injections. **Hæmoptysis** occurred as a sequel of the first injection in one case (15), but did not recur on a repetition. In another of pulmonary disease (Case 31) it occurred after the fourteenth injection.

Improvement of varying degree, in some absolute, in others symptomatic, took place in fourteen cases (Nos. 3, 8, 9, 10, 12, 14, 16, 17, 18, 19, 20, 21, 24, 25, and 30). In two of these (3 and 8) treatment was discontinued on account of enfeebled state of the patient's general health, and consequent absence of rallying power. In two also (3 and 17) death took place, one from pernicious anaemia, in the other from extensive laryngeal and pulmonary tuberculosis, so that only ten, or one half, of the cases are to be credited with real improvement. In one (25) there was no further development, but, on the contrary, an improvement of already existing infiltration and catarrh.

Progress is not reported in four cases (4, 11, 22, and 23), too short a time having elapsed for observation. **No improvement**, even of symptoms, was observed in two instances (13 and 15).

As to **new growths** or excrescences, my series shows progressive absorption in only one case (16), though the same process was observed in several instances of simple infiltration; but others have been reported of the rapid necrosis and disappearance of absolute growths on the vocal cords—one by Professor Von Bergmann, to which I allude at page 16, and another under the care of Professor Oppenheimer, of Heidelberg.

Finally, it is to be remarked, with regard to Class III., that in the three cases I saw in Berlin, and the four I have myself treated—seven in all—the value of the remedy as an aid to diagnosis is incontestable, and it is difficult to understand the type of mind that will not concede this point. Those here detailed are very interesting. In one (25) analeptic measures were proved to have subdued an incipient pulmonary and laryngeal tuberculosis; in a

second (29), intra-laryngeal surgical measures of curettage and lactic acid were proved to have been successful; in a third (27), a suspicion of tuberculosis, without physical signs, was confirmed; and in a fourth (Case 31), a suspicion of extension of the disease beyond the limits detected by physical examination, was proved to have had no foundation in fact. Of the other three, one (26) gave satisfactory evidence—with a promise of cure—that a doubtfully malignant disease was a benign lupus; in a second (Case 30), the suspected tuberculous nature of enlarged cervical glands was verified, and the disease itself ameliorated; while in the last (Case 29), the presumption that an ulcer on the pharynx of a patient with pulmonary tuberculosis was syphilitic gained strong confirmatory support.

Concluding Remarks.—I venture to hope that the foregoing summary, which I have endeavoured to make strictly impartial, will be held to justify my previous attempts to explain the clinical phenomena of the remedy; and that the whole will be admitted to satisfactorily demonstrate a fulfilment of the threefold purpose of the essay as announced in my preface. I trust also it will be admitted that the results already obtained by Koch's remedy in throat consumption are such as to warrant us to persevere in its employment, provided always that due caution be exercised not only in the selection of patients for its application, but also in every detail of its administration.

APPENDIX.

(From THE BRITISH MEDICAL JOURNAL, January 17, 1891.)

A FURTHER COMMUNICATION

ON A

REMEDY FOR TUBERCULOSIS.

BY PROFESSOR DR. ROBERT KOCH,

BERLIN.

[The German text from which this is translated is published in the DEUTSCHE MEDICINISCHE WOCHENSCHRIFT, January 15, 1891.]

RESULTS OF RECENT THERAPEUTIC EXPERIENCE.

SINCE the publication of my experiences with a new remedy for tuberculosis two months ago, many doctors have been put in possession of the remedy, and have thus been enabled to make themselves acquainted with its qualities by their own experiments. As far as I can judge by the publications that have appeared on the subject, and the letters addressed to me, my statements have, on the whole, found full confirmation. That the remedy exercises a specific action on tuberculous tissue, and can in consequence be employed as a very delicate and certain reagent in searching out hidden, and diagnosing doubtful, tuberculous processes, is agreed on all sides. And in regard also to the therapeutic effect of the remedy, most accounts agree that, in spite of the relatively short duration of the treatment, many patients show improvement, varying only in degree. In not a few cases I am informed that cure even has been attained. Only in some exceptional cases has it been affirmed that the remedy may not only be dangerous in too far advanced cases—which is freely admitted—but that it directly hastens the tuberculous process, that it is, in fact, harmful *per se*. I myself have had the opportunity during a month and a half of collecting further experiences regarding the therapeutic effect and the diagnostic value of the remedy in about 150 cases of various forms of tuberculosis, and I can only say that all I have lately seen is in harmony with my former observations, and that I have nothing to retract of what I have before stated.* So long as the only point of importance was to judge of the correctness

* As regards the duration of cure, I should like to state here that of the cases which I had provisionally marked cured, two have been again received into the Moabit Hospital for further observation, and that for three months no bacilli have been present in their sputum; the physical signs, too, have gradually quite disappeared.

of my statements, it was not essential to know what the remedy contains, and what its origin is. On the contrary, it was clear that subsequent experiments would be all the more unprejudiced the less was known of the remedy itself; but now that such experiments in sufficient number have been made, and have proved the importance of the remedy, the remaining task is to study the remedy beyond the application it has hitherto found, and, if possible, to apply the principles which lie at the foundation of its discovery to other diseases. This task, of course, demands a full knowledge of the remedy.

THE STEPS BY WHICH THE DISCOVERY WAS MADE.

I therefore think the right moment has come to make the necessary statements which follow, before I discuss the remedy itself. I think it imperative for the better understanding of its action to trace shortly the steps that led me to its discovery. If a healthy guinea-pig be inoculated with a pure cultivation of tubercle bacilli, the inoculation wound generally becomes sealed, and seems to heal up during the next few days. It is only in the course of from ten to fourteen days that a hard nodule is formed, which soon opens, forming an ulcerating spot which persists until the death of the animal; but the case is very different if an already tuberculous animal be inoculated. The most suitable animals for this experiment are those that have already been successfully inoculated four to six weeks previously. In the case of such an animal also the small inoculation wound becomes sealed at first, but no nodule is formed, a peculiar change taking place at the point of inoculation. Already, on the first or second day, the spot becomes hard and dark-coloured; and this is not confined to the point of inoculation, but spreads around to a diameter of 0·5 to 1 centimetre. During the next few days it becomes more and more clear that the epidermis thus changed is necrotic. Finally it is thrown off, and a flat ulcerated surface remains, which generally heals quickly and completely, without carrying infection to the neighbouring lymphatic glands. Thus the inoculated tubercle bacilli act quite differently on the skin of a healthy guinea-pig and on that of a tuberculous one. But this remarkable action does not belong exclusively to living tubercle bacilli, but also in the same degree to dead ones, whether killed by low temperatures of long duration, which I at first tried, or by boiling heat, or by certain chemicals.

This peculiar fact having been ascertained, I followed it up in all directions, and it was then further found that pure cultivations of tubercle bacilli thus killed, after they have been ground down and suspended in water, can be injected under the skin of healthy guinea-pigs in large quantities without producing anything but local suppuration.* Tuberculous guinea-pigs, on the other hand, can be killed by an injection of very small quantities of such suspended cultures, the time being from six to forty-eight hours, according to the dose; a dose which is just insufficient to kill the animal is sufficient to produce a widespread necrosis of the skin in the region of the point of inoculation. If the suspended matter be still more diluted, so that it is scarcely turbid to the eye, the animals remain alive; and if the injections be continued at intervals of one or two days, a noticeable improvement in

* Injections of this nature are among the simplest and most certain methods of producing suppuration free from living bacteria.

their condition soon sets in ; the ulcer at the point of inoculation becomes smaller, and finally cicatrizes. This is never the case without such treatment. The swollen lymphatic glands become smaller, the condition as regards nutrition improves, and the progress of the disease is arrested, if it is not already so far advanced that the animal dies of debility.

DIFFICULTIES IN THE WAY OF THE THERAPEUTIC APPLICATION.

These facts formed the foundation of a therapeutic method against tuberculosis. But an obstacle to the practical employment of such suspensions of killed bacilli was found in the phenomenon that the tubercle bacilli are by no means reabsorbed, nor do they disappear in any way, but for a long time remain unchanged in their position, producing smaller or larger suppurating centres. Thus it was clear that in this method the curative effect on the tuberculous process is obtained by a soluble substance, diffused, so to speak, into the fluids that surround the tubercle bacilli, and transferred without delay to the circulating fluids of the body, whereas that which has the pus-forming quality seems to remain behind in the tubercle bacilli, or at any rate to be only very slowly dissolved. Thus the only important thing to be done was to carry out the process, which takes place within the body—*outside* of it also—and if possible to extract and isolate the curative substance from the tubercle bacilli. This problem required much work and time before at last I succeeded, by the help of a 40 to 50 per cent. solution of glycerine, in extracting the active principle from the tubercle bacilli. My further experiments on animals, and finally on human beings, were made with liquid thus obtained ; and in this way also the liquid which I let other physicians have in order to repeat the experiments was obtained. The remedy with which the new therapeutic treatment of tuberculosis is carried out is, therefore, a glycerine extract of pure cultivations of tubercle bacilli.

THE COMPOSITION OF THE REMEDY.

Besides the active principle there pass from the tubercle bacilli into the simple extract all other substances soluble in 50 per cent. glycerine, and therefore there is found in it a certain quantity of mineral salts, pigment, and other unknown extractive substances. Some of these substances can be removed from it without difficulty, for the active principle is insoluble in absolute alcohol, and can be precipitated by it—not pure, it is true, but in combination with other extractive substances likewise insoluble in alcohol. The colouring matter, too, can be separated out, so that it is possible to obtain a colourless dry substance from the extract which contains the active principle in a much more concentrated form than the original glycerine solution. But this purifying of the glycerine extract has no advantages as regards practical application, as the substances thus removed have no action on the human organism, and the process of purifying would, therefore, only cause unnecessary expense. The constitution of the active principle can as yet be only a matter of conjecture. It seems to me to be a derivative of albuminous bodies, and to be in close relation to them ; but it does not belong to the group of so-called toxalbumins, as it can withstand high temperatures, and in the dialysator passes quickly and easily through the membrane. The quantity of

active principle present in the extract is, in all probability, very small ; I estimate it at fractions of 1 per cent. Thus, if my assumption be correct, we have to deal with a substance the action of which on the tuberculous organism far surpasses that of the strongest drugs known.

PROBABLE MODE OF ACTION OF THE REMEDY.

Various hypotheses may, of course, be formed as regards the specific mode of action of the remedy on tuberculous tissue. Without in any way affirming that my view is the best possible explanation, I imagine the process to be as follows : The tubercle bacilli in their growth produce in the living tissues—just as in the artificial cultivation—certain substances which have various but always deleterious influences on the living elements of their surroundings—the cells. Amongst these substances is one which, in a certain concentration, destroys living protoplasm, and causes it to undergo a transformation into the condition called ‘coagulation-necrosis’ by Weigert. The tissue having become necrotic, this condition is so unfavourable to the nutrition of the bacillus, that it is unable to develop further, and finally in some cases it dies off. In this way I explain the remarkable phenomenon that in organs freshly attacked by tuberculous disease—for instance, in a guinea-pig’s spleen or liver filled with grey nodules—numerous bacilli are found, whilst bacilli are rare or entirely absent when the enormously enlarged spleen consists almost entirely of whitish substance in a condition of coagulation-necrosis, such as is often found in guinea-pigs which die of tuberculosis. A solitary bacillus, however, cannot produce necrosis at a great distance, for as soon as the necrosis has reached a certain extent the growth of the bacillus, and, in consequence, the production of the necrosis-producing substance, diminishes, and thus a sort of mutual compensation sets in, and to this it is due that the growth of isolated bacilli is so remarkably restricted, as, for example, in lupus, in scrofulous glands, etc. In such cases the necrosis only extends over a part of the cell, which then, in its further growth, assumes the peculiar form of a giant cell ; I thus follow in this statement of my views the explanation of the growth of giant cells first given by Weigert. Now, if the necrosis-producing substance were artificially added to that contained in the tissue surrounding the bacillus, then the necrosis would extend further, and thus the conditions of nutrition of the bacillus would be much more unfavourable than is usually the case. Then, not only would the more completely necrosed tissues disintegrate, slough, and—where this is possible—take with them the enclosed bacilli, carrying them outward ; but the bacilli would also be disturbed in their growth to such an extent that they would die off much sooner than is the case under ordinary conditions. It is in calling forth such changes that, to my mind, the action of the remedy seems to consist. It contains a certain amount of the necrosis-producing substance, of which a correspondingly large dose has a deleterious influence—even in healthy persons—on certain elements of the tissues, probably on the white blood corpuscles or cells closely related to them, thus giving rise to the fever and the whole peculiar complex symptoms. In tuberculous persons a much smaller quantity suffices to cause, at certain spots—that is, wherever tubercle bacilli vegetate and have already impregnated their surroundings with the necrosis-pro-

ducing substance—a more or less extended necrosis of cells with the accompanying symptoms affecting the entire organism. In this way it is possible to explain—at least for the present—in a provisional way the specific influence which the remedy in certain well-recognised doses exercises on tuberculous tissue, as well as the possibility of increasing the doses in so remarkable a fashion, and, finally, to explain the curative effect which the remedy undoubtedly possesses where the circumstances are at all favourable.

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